IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

SEAGEN, INC.,	(	CAUSE NO. 2:20-CV-337-JRG
	)	
Plaintiff,	(	
	)	
vs.	(	
	)	
DAIICHI SANKYO CO., LTD.,	(	
	)	
Defendant, and	(	
	)	
ASTRAZENECA PHARMACEUTICALS, LP and ASTRAZENECA UK, LTD.,	(	MARSHALL, TEXAS
	)	
	(	APRIL 6, 2022
Intervenor-Defendants.	)	8:30 A.M.

VOLUME 3

TRIAL ON THE MERITS

BEFORE THE HONORABLE RODNEY GILSTRAP
UNITED STATES CHIEF DISTRICT JUDGE
and a jury

SHAWN McROBERTS, RMR, CRR
100 E. HOUSTON STREET
MARSHALL, TEXAS 75670
(903) 923-7464
shawn_mcroberts@txed.uscourts.gov

A P P E A R A N C E S

FOR THE PLAINTIFF:

MORRISON & FOERSTER, LLP
SAN FRANCISCO
425 MARKET ST., 32ND FLOOR
SAN FRANCISCO, CA 94105-2482
(415) 268-7000
BY: MR. MICHAEL JACOBS
MR. MATTHEW CHIVVIS

MORRISON & FOERSTER, LLP
PALO ALTO
755 PAGE MILL ROAD
PALO ALTO, CALIFORNIA 94304
(650) 813-5600
BY: MR. BRYAN WILSON
MR. SUMAIYA SHARMEEN

WARD, SMITH & HILL, PLLC
1507 BILL OWENS PARKWAY
LONGVIEW, TX 75604
(903) 757-6400
BY: MR. JOHNNY WARD
MR. WES HILL
MS. ANDREA FAIR

FOR THE DEFENDANT:

PAUL HASTINGS, LLP - NEW YORK
200 PARK AVENUE
NEW YORK, NY 10166
(212) 318-6055
BY: MR. PRESTON RATLIFF, II

THE DACUS FIRM, PC
821 ESE LOOP 323, SUITE 430
TYLER, TX 75701
(903) 705-1117
BY: MR. DERON DACUS

MANN TINDEL & THOMPSON
201 E. HOWARD STREET
HENDERSON, TX 75654
(903) 657-8540
BY: MR. MARK MANN

FOR THE INTERVENORS:	WILLIAMS & CONNOLLY, LLP - WASHINGTON 725 TWELFTH STREET, N.W. WASHINGTON, DC 20005-5901 (202) 434-5000 BY: MR. DAVID BERL MS. JESSAMYN BERNIKER MS. JESSICA PAHL MS. KATHRYN KAYALI MR. TOM FLETCHER MR. NICK ROBERTS
	WILSON ROBERTSON & CORNELIUS ONE AMERICAN CENTER 909 ESE LOOP 323, SUITE 400 TYLER, TX 75711-7339 (903) 509-5000 BY: MS. JENNIFER AINSWORTH
OFFICIAL REPORTER:	SHAWN M. McROBERTS, RMR, CRR 100 E. HOUSTON STREET MARSHALL, TEXAS 75670 (903) 923-8546

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EXAMINATION

THE COURT: Please be seated.

Ms. Ainsworth, does the Defendant care to make some proffer into the record?

MS. AINSWORTH: Your Honor, with the Court's permission, if we could do that either right before or after the lunch break, we would appreciate it.

THE COURT: That will be fine. Just remind me and let me know when you're ready to do so.

MS. AINSWORTH: Thank you, Your Honor.

THE COURT: Are the parties prepared to read into the record those items from the list of pre-admitted exhibits used during yesterday's portion of the trial?

MS. STAURING: Yes, Your Honor.

THE COURT: Please proceed.

MS. STAURING: Good morning, Your Honor. Jessica Stauring on behalf of Defendants.

THE COURT: Please proceed.

MR. HAN: Good morning, Your Honor. Chris Han on behalf of Plaintiff.

MS. STAURING: The parties have agreed to read the following exhibits into the records. The next exhibits are all PX: 2, 19, 20, 21, 34, 35, 36, 37, 73, 93, 151, 157, 158, 160, 161, 163, 168, 180, 184, 208, 209, 210, 211, 212, 227, 230, 235, 247, 256, 374, 405, 411, 521, 523, 536, 538, 549, 566, 575, 653, 724, 745, 758, 849, 856, 869, 878, 905, 971,

975, 978, 1008, 1014, 1049, 1137, 1139.

The following exhibits are all DX: 63, 113, 114, 123, 286, 694, 941, 961, 990, 1142, and 1151.

That's all, Your Honor.

THE COURT: Any objections from the other side?

MR. HAN: Nothing from Plaintiff, Your Honor.

THE COURT: All right. Thank you, counsel.

MS. STAURING: Thank you, Your Honor.

THE COURT: I don't want to interfere with complete hydration during the trial, but could we take the water bottles off the bar? I don't want them just -- we don't want things stacking up there.

Okay. Is there anything we need to take up additionally before I bring in the jury?

MR. JACOBS: Nothing from Seagen, Your Honor.

MR. DACUS: Nothing from Defendants, Your Honor.

THE COURT: All right. Could we get Doctor Naito and the interpreter back at the witness stand?

And you may go to the podium and prepare, Mr. Jacobs.

And I remind you both, you remain under oath.

THE INTERPRETER: Yes, Your Honor.

THE COURT: Good morning.

All right, Mr. Johnson, would you bring in the jury, please?

(Whereupon, the jury entered the courtroom.)

THE COURT: Good morning, welcome back. It's good to see you. Please have a seat.

We'll continue with Doctor Naito where we left off yesterday, and we are proceeding with cross-examination of the witness by Plaintiff's counsel.

Mr. Jacobs, you may proceed.

MR. JACOBS: Thank you, Your Honor.

HIROYUKI NAITO, PhD., PREVIOUSLY SWORN,

CROSS EXAMINATION continued

BY MR. JACOBS:

Q. Good morning, Doctor Naito, and congratulations on your work.

A. Good morning. Thank you.

Q. Doctor Naito, you did not begin the development of Enhertu from scratch. Correct?

A. The Enhertu research for me began with the past DDS research that was conducted in the -- towards the end of the 1990s, and that is what I applied to my research.

Q. Well, others had done work on the project that ultimately led to Enhertu. Correct, Doctor Naito?

A. Well, I was the one that first discovered and invented the overall structure of Enhertu, but prior to my joining the ADC project, the project was already underway.

Q. You joined the ADC working group in January 2011. Correct?

A. Yes, my recollection is that it was around that time.
Q. By the time you joined in January 2011, the team had already developed an antibody-drug conjugate linker. Correct?
A. There were some ADCs that had already been synthesized and were being evaluated.
Q. The linker that was provided to you by the project team had an MC group to connect the linker to the antibody. True, sir?
A. Yes. By the time I joined, that kind of work had the taken place.
Q. The linker had a cleavable peptide sequence GGFG already. True, sir?
A. Yes. By the end of the 1990s in the DDS research that was ongoing at the company, the tetrapeptide sequence GGFG had already been found, discovered, and was being used.
Q. Sir, please listen carefully to my question. In the work that was provided to you by the team, the linker already had a cleavable peptide sequence GGFG. True, sir?
A. Yes, it was.
Q. And the project team was already working with a drug compound DX-8951. True, sir?
A. Yes, they were already working with that.
Q. Let's take a look at the structure of Enhertu.
MR. JACOBS: Mr. Lee, could we have slide 8 from Doctor Naito's presentation up, please? That's marked DDX

2-9.

Q. (BY MR. JACOBS) Now, Doctor Naito, moving from left to right on the structure of Enhertu, let's start with the antibody, and my question for you is, what antibody is on Enhertu?

A. It is a HER2 antibody.

Q. In fact, the antibody is trastuzumab. Correct, sir?

A. That's right.

Q. And trastuzumab is a monoclonal antibody developed by GenenTech. True, sir?

A. I'm sorry. I'm not familiar to that extent.

Q. You did not develop the antibody that is shown on your slide DDX 2-9. Right?

A. Yes. The antibody is not something that I developed.

Q. Moving further over to the right, you were not involved in the cysteine conjugation of the linker to the sulfur atom of the anti-HER2 antibody. Correct, sir?

A. Correct. I was not involved in that.

Q. And you did not perform the step of conjugating the drug linker to the cysteine residue of the antibody to make Enhertu.

A. Correct. That's not something I did directly myself.

Q. And if we point to that portion on your slide, Doctor Naito, with a red circle that we have added --

MR. JACOBS: Mr. Lee, the next. That's fine. Thank

you.
Q. (BY MR. JACOBS) That work was already done by the time you joined the project team. Right, sir?
A. Yes, it was.
Q. Moving further to the right, the GGFG tetrapeptide, we talked about that that work was already done by the team by the time you joined. Right, sir?
A. Yes. Drawing on past knowledge gained, it was already being used.
Q. You don't know for a fact where the working group came up with GGFG, do you, sir, because you were not part of the working group at that time?
A. That's true. I hadn't heard exactly how they came up with it, but the DDS research that used this that was done in the late 1990s is something that I was a part of and how GGFG came to be used thereafter is also something that I do know something about.
Q. Moving all the way over to the right, sir, DX-8951, that drug unit was already a part of the proposed antibody-drug conjugate when you joined the team. Right, sir?
A. Yes, that's correct.
Q. And the work that led to the choice of a DAR of 8 for Enhertu, that work was done by others. True, sir?
A. On that, I don't have a clear recollection. That could have taken place after I joined. I'm not sure. But my

recollection is that there had not yet been actual results, a record showing that that worked.

Q. You yourself did not select the DAR of 8. Correct?

A. I myself did not select 8.

Q. I'm sorry?

A. Did not select 8. I myself did not.

Q. Now, even as to what you've denoted the spacer on your graphic, by the time you joined the working group, there had been some partial work on a spacer which was similar to the spacer you worked on. True, sir?

A. I don't recall whether that work had already been done by the time I joined. However, after I did join the team, some work did take place using a spacer that was similar to mine.

Q. And that work was done by others. True, sir?

A. Yes, in part it is work that others did.

Q. I'd like to ask you to look at a couple of scientific publications coming out of the Enhertu project at Daiichi Sankyo. Let's take a look first at PX 299.

And, Doctor Naito, if you want to look at it, it's in this binder called Naito Cross Exhibits. It will also be up on the screen.

A. I see it.

Q. Now, this is one of the first papers describing DS-8201, the project that became Enhertu. True, sir?

A. Just looking at it right now, I can't tell you exactly,

but it does appear to be a publication issued by Daiichi Sankyo.

Q. Well, you recognize the names of the authors on that paper. True, sir?

A. I recognize a number of the names.

Q. Your name is not shown as one of the authors on this paper. True, sir?

A. Correct, my name does not appear there.

MR. JACOBS: Just so we get the dates of this paper clear for everyone, can we show that date call-out at 10, Mr. Lee?

Q. (BY MR. JACOBS) Look down at the bottom there. Does that help you remember, Doctor Naito, this is one of the first papers describing DS-8201, the antibody-drug conjugate that became known as Enhertu?

A. I can't be certain. I can't necessarily agree with you because I don't have a clear recollection as to whether I've seen this article.

Q. On this authors' contributions, you will see again you are not listed as one of the contributors. Do you observe that, sir?

A. If -- could I have a moment to look through this? That's correct. I don't see my name there.

MR. JACOBS: Mr. Lee, could we have slide 7 from Doctor Naito's slides yesterday?

Q. (BY MR. JACOBS) Doctor Naito, you testified that this is the molecule, the molecule on the right there, is the molecule you synthesized from November 18th to November 28th, 2011. Right?

A. Yes.

Q. But, in fact, sir, this structure shown in the red box on your slide is not Enhertu or DS-8201, the antibody-drug conjugate at issue in this case, is it, sir?

A. This itself is not Enhertu.

Q. I'm sorry. I'm having a little trouble hearing you?

A. This itself is not Enhertu.

Q. Because it's missing the antibody. Correct, sir?

A. Right. There is no antibody there.

Q. So you are not, in fact, the first person to invent the overall structure of Enhertu. True, sir?

A. I am the one that thought of the overall structure for the first time. What characterizes the overall structure of Enhertu is the structure of the drug linker, and I am the one that first thought of it.

Q. Now, Doctor Naito, turning to some of the issues in the case about infringement, Enhertu is an antibody-drug conjugate that is internalized into cancer cells to release DXd inside the cell. Right?

A. Yes. What is released is DXd, which is DX-8951 to which a part of the spacer hydroxyacetone is attached.

Q. And that means that Enhertu is intracellularly cleaved to release the drug DXd. Correct, sir?
A. After it is broken down inside of the cell, DXd is released.
Q. And that means that DXd is released after intracellular cleavage. True, sir?
A. Could I hear that question again?
Q. That means that DXd is released after intracellular cleavage.
THE INTERPRETER: I'm sorry. The interpreter has a question. Is there a difference between intercellular and intracellular?
MR. JACOBS: Inside, intra.
Q. (BY MR. JACOBS) Doctor Naito, I withdraw the question.
Doctor Naito, do you understand the English expression intracellular cleavage?
A. Well, I'm not a biologist, so I can't say that I, you know, know it very well clearly, but I think I understand what you're saying, you're talking about.
Q. It is true that DXd is released into the cancer cell after intracellular cleavage of the Enhertu antibody-drug conjugate.
A. I feel as though I have heard that, but as I said, I am not a biologist, and so I cannot say to you for certain whether that is the case or not. I don't know.

Q. Let's take a look at another one of your slides, sir. Let's take a look at your slide 2 from yesterday.

In this slide you show that after release, after cleavage, part of the spacer remains attached. Do you see that?

A. I see that.

Q. The spacer is part of the linker. Correct, sir?

A. No, it is not part of the spacer. It is not -- sorry. No, it is not part of the linker. It is the spacer.

Q. So now you're going to -- you contend that the spacer is not part of the linker of the drug to the antibody, sir?

THE INTERPRETER: I'm sorry. I may have messed up the translation. Can you ask the question again?

Q. (BY MR. JACOBS) Let me ask the question again. Is it your contention before the jury, Doctor Naito, that the spacer is not part of the linker that connects the drug to the antibody?

A. I believe when I gave my explanation regarding the overall structure of Enhertu, I said that it was comprised of four parts, and one of those parts is the spacer. So going back to your question, I think the correct expression would be to say that the spacer is a part of the drug linker.

Q. Now let's take a look at the presentation you gave to scientists in 2019 at Daiichi Sankyo looking back on your work on Enhertu. And this is PX 169 in Japanese and PX 170 in

English. And let's take a look at page 3.
A. Yes, I see that.
Q. And in the middle, sir, we have DXd. Correct, sir?
A. Yes, there is.
Q. And you're showing how DXd is released when Enhertu is internalized. Correct, sir?
A. That was not the reasoning behind the preparation of this slide.
Q. But you are showing that.
A. I would like to answer correctly, so could you repeat the question again?
Q. Let me ask a slightly different question. The green box at the bottom where it's labeled 'neutral', that is DXd. Correct, sir?
A. Yes, this is DXd.
Q. And in this slide in your internal presentation before this lawsuit, you wrote with an exclamation point, "No linker!" Correct, sir?
A. Yes, in Japanese I wrote, "No linker!"
Q. Thank you, Doctor Naito.
A. This is something that I prepared so I will explain to you what this means.
Q. Maybe when your counsel gets back up, you can do that, sir, but for now I want to move on to another topic.
THE COURT: Mr. Jacobs, if the witness becomes

non-responsive, even in a different language, raise it with me and I'll instruct the witness.

MR. JACOBS: Thank you. Judge Gilstrap, please instruct the witness.

THE COURT: The witness needs to limit his answers to the questions asked, and if he feels further explanation is necessary, that is the job for opposing counsel to raise when they have a further opportunity to ask questions.

THE WITNESS: I understand, Your Honor.

THE COURT: Thank you. Let's proceed.

Q. (BY MR. JACOBS) And just for clarity, Doctor Naito, when we talk about DXd, we're talking about the drug that is the actual chemotherapeutic that treats the cancer after cleavage. Right, sir?

A. Yes. It is what is released from Enhertu.

Q. DXd was also known inside Daiichi Sankyo as RDD-1166?

A. I'm sorry. I don't remember the exact number.

Q. When DXd is released in the cell after cleavage, it is a free drug. True, sir?

A. I'm sorry. I didn't understand the meaning of your question.

Q. Do you understand the expression in English 'free drug', sir?

A. I wasn't able to understand that.

Q. I'm sorry. Could you give me the answer again?

A. I wasn't able to understand that.
Q. Is yakubutsu a phrase you understand, sir?
A. I understand yakubutsu.
THE INTERPRETER: But the interpreter would say that that would be translated as released drug in English. Is that right?
Q. (BY MR. JACOBS) Sir, let me ask you about a paper that you were involved in. This is PX 263, and let's look at the first page of that.
THE INTERPRETER: I'm sorry to interrupt, but there has been something that's been on my mind and I'm wondering if it's appropriate for me to say, going quite a back a few questions, but it's still on this page of mine. I'm not sure if I may have made an interpreting mistake.
Is that something I can check now or is that something I do later?
MR. JACOBS: Could we have a quick sidebar perhaps, Judge Gilstrap, with the two interpreters?
THE INTERPRETER: I would just need to go look back at the record and compare it against my notes.
THE COURT: Take a moment and look at the record and compare it with your notes. And if, having done that, you believe you've made a mistake, let me know. If you believe there's no mistake, then please let me know that.
THE INTERPRETER: Thank you, Your Honor.

THE COURT: Please take a moment.

THE INTERPRETER: Thank you, Your Honor.

Is this something that I can double-check with the witness or the other interpreter perhaps?

THE COURT: No. If you think you've made a mistake from your notes, then let me know. If you're not sure, then we'll just move on.

THE INTERPRETER: I believe that the witness said that the word -- that the drug linker would be -- it would be more accurate to say that the drug linker is a part of the spacer. Does that make sense?

Q. (BY MR. JACOBS) Doctor -- let's just do this again.

THE COURT: Go ahead, counsel.

Q. (BY MR. JACOBS) Doctor Naito, does an antibody-drug conjugate consist of three parts--an antibody, a linker, and a drug?

A. Could I hear that question again?

MR. JACOBS: Court reporter, could you please read it back?

THE COURT REPORTER: "Doctor Naito, does an antibody-drug conjugate consist of three parts--an antibody, a linker, and a drug?"

THE WITNESS: When you say ADC, I don't know exactly what you're talking about. If you're talking about Enhertu, it is comprised of four parts, as I've said before--the

antibody, the linker, the spacer, and the drug unit.

Q. (BY MR. JACOBS) Now let me ask my question again about whether DXd, the drug that is released on cleavage, is a free drug.

A. And when you say free drug, what do you mean?

Q. Well, let's take a look at your paper again, PX 263.

MS. MAYS-WILLIAMS: Your Honor, at this moment it seems we may be moving into some confidential information of the Defendants, and if we are, we would like to seal the courtroom.

THE COURT: All right. Based on counsel's request and to protect confidential information, I'll order the courtroom sealed.

I'll direct that all persons present who are not subject to the protective order that's been entered in this case should excuse themselves and remain outside the courtroom until it is reopened and unsealed.

(Courtroom sealed.)

(Courtroom unsealed.)

THE COURT: All right. Defendants, call your next witness.

MS. AINSWORTH: Your Honor, Defendants call as their next witness Dr. Scott Jeffrey by video deposition. Dr. Scott Jeffrey is a senior director of chemistry at Seagen.

The video is 15 minutes and 47 seconds long. Defendant's designations are 13 minutes and 14 seconds, and Plaintiff's designations are 2 minutes, 33 seconds.

THE COURT: Proceed with this witness by deposition.

MS. AINSWORTH: And there are three exhibits that will be used with the video. They are DX 490, DX 495, and DX 571.

THE COURT: All right. Let's proceed with the video deposition.

SCOTT JEFFREY, PhD., BY SWORN VIDEO DEPOSITION,

Q. Doctor Jeffrey, what's your current position at Seattle Genetics or your position before you went on leave?

A. I still hold that position. I'm senior director of chemistry.

Q. What year did you join Seattle Genetics?

A. 2002.

Q. Seagen didn't invent the concept of an antibody-drug

conjugate. Correct?
A. That's correct.
Q. Seagen didn't invent the idea of conjugating a drug to an antibody.
A. That's correct.
Q. And Seagen didn't invent the idea of using an antibody-drug conjugate to treat cancer. Right?
A. That's correct.
Q. And Seagen didn't invent the use of a maleimidocaproyl group to conjugate a drug linker to an antibody. Right?
A. They were not the first ones to do that.
Q. And Seagen didn't invent the use of a maleimidocaproyl group to conjugate a drug linker to a cysteine residue in an antibody. Right?
A. That's correct.
Q. Seagen didn't invent the use of a cleavable peptide in a drug linker in an ADC. Right?
A. That's correct.
Q. In what context was the first time you saw an ADC containing a drug linker with a tetrapeptide composed only of glycine and phenylalanine residues?
A. It was -- it was likely associated with the DS-82 -- 8201 molecule.
Q. What is DS-8201?
A. That's Herceptin conjugated to a tetrapeptide

camptothecin drug linker, Enhertu.

Q. And the first time you ever saw an ADC with a tetrapeptide composed only of glycine and phenylalanine residues was in Enhertu. Right?

A. I believe so.

Q. Have you ever synthesized a drug linker for an ADC containing a tetrapeptide composed only of glycine and phenylalanine residues?

A. I don't think so.

Q. In the intervening time between when you started at Seattle Genetics in 2002 and the first time that you saw DS-8201, you never saw in any context, in a lab meeting, in anybody's lab notebook, in any document, an ADC with a tetrapeptide linker composed only of glycine and phenylalanine residues. Right?

A. Not that I can recall.

Q. So you were aware of the structure of DS-8201, at least as of May 2016?

A. Yep.

Q. And as of November 7, 2016, the chemistry department at Seagen was familiar with the preclinical and clinical results for DS-8201. Right?

A. Yeah. I mean, sure.

Q. Sure. At the time you were doing your camptothecin work, did you understand Seattle Genetics to possess drug linkers

containing tetrapeptides composed of glycine and phenylalanine residues?

A. We did not.

Q. Doctor Jeffrey, I'm handing you what I've marked as Exhibit No. 11 to your deposition, a document the first page of which has the Bates number SGIEDTX00166018. This is an email from you to some of your colleagues in chemistry research, including Peter Senter, Nicole Oakley, David Meyer, Robert Lyon, Ryan Lyski, and Uland Lau, dated March 9, 2017. Do you see that?

A. Uh-huh.

Q. And the subject was Camptothecin Assessment. Do you see that?

A. Yep.

Q. And you wrote, Ryan and Uland have put together a nice cassette of camptothecin drug linkers.

What was the cassette of camptothecin drug linkers?

A. That's just a series of drug linkers and a number of different examples.

Q. Okay. Including Immunomedics' and Daiichi Sankyo's drug linkers. Do you see that?

A. Yep. We synthesized both Immunomedics and the Daiichi Sankyo linker, yes.

Q. In 2017, or any time before or after this email, did Peter Senter ever come to you and say, I invented drug linkers

containing tetrapeptides composed of solely glycine and phenylalanine residues?

A. No.

Q. He didn't ever email you back after this email and say, you know, Doctor Jeffrey, that should say Peter Senter's drug linker?

A. He did not.

Q. Doctor Jeffrey, I'm handing you what I've marked as Exhibit 12 to your deposition, which is a document, the first page of which has the Bates number 16 -- SGIEDTX00165845. And this is an email from you to Peter Senter, copying Doctor Burke. Do you see that?

A. Yeah. Let me look at this real fast. Okay.

Q. And the group meeting presentation would have been a presentation -- the chemistry group meeting presentation Ryan gave?

A. Yes.

Q. And a few more slides in on the page ending with the Bates ending in 165857, there's a slide title Camptothecin Peptide Library.

A. Yeah.

Q. When you were doing this work, did you understand Doctor Senter to have invented this set of peptides for use in a drug linker in 2004?

A. Not -- not these specific sequences.

Q. Did you understand Daiichi Sankyo to have invented these drug linkers?
A. These -- the ones that are listed under Daiichi Sankyo linker analogs? I -- I didn't understand them to have invented those. So I don't know. And I know that structures similar to this where -- yeah. I know there was some papers and I know there was a -- I mean, we're talking specifically in the context of ADCs right now. I know there was some earlier papers by Daiichi where they -- they may have looked at these sequences. I don't know for sure, though.
Q. As of September 13, 2019, SGD-7782 was the culmination of 15 years of work on camptothecin ADCs at Seagen. Right?
A. I don't -- I don't know about the -- the metric 15 years. It was -- it was the -- it was a drug linker that -- it was -- it was a camptothecin drug linker that had advanced the furthest at the time in our -- in our corporate history.
Q. And this was a lot of work.
A. In -- in looking at the bandwidth of the group as a whole through time, the camptothecins, even when they were being staffed at their highest level, wasn't a significant portion or wasn't a majority of -- of the chemistry effort going on in the chemistry group.
Q. This was --
A. So there -- there was definitely some -- some research effort that went into camptothecins.

Q. What happened to SGD-7782?
A. We dropped it due to tox reasons.
Q. It's really hard to develop an ADC. Right? That can make it to even preclinical candidate nomination. Right?
A. Not always.
Q. This was difficult. Right?
A. This was difficult. Can you be specific about what you mean by 'this'?
Q. This was the culmination of a substantial effort by your group to develop a preclinical candidate ADC. Right?
A. It was a lead we brought forward that there was significant interest in.
Q. And in developing SGD-7782, you had access to all of Seagen's prior publications. Right?
A. Yeah.
Q. You had access to all of Seagen's prior patents. Right?
A. I did have access, yes.
Q. Yeah. And you had access to all of Seagen's internal trade secrets relating to ADCs, all the internal work. Right?
A. Potentially would have access to those, yes.
Q. And so this was the result of Seagen, one of the world's leading companies in ADCs, attempting to develop a new camptothecin-containing ADC and it was a failure. Right?
A. There was a judgment call about whether to develop the molecule. I -- I wouldn't characterize it necessarily as a

failure.
Q. If Peter Senter invented a technology by which any unpublished could be linked to any drug, including a camptothecin, via a tetrapeptide linker composed of glycine and phenylalanine residues in 2004, why didn't he ever tell you to do that?
A. Well, I -- I wasn't working on camptothecins at that stage, so that would have been outside the scope of what he had asked me to work on.
Q. And you've worked for Doctor Senter, either directly or with someone intervening, but he's been your ultimate supervisor for the entire time you've been at Seagen, and he never once told you, Doctor Jeffrey, you know what you should do? You should synthesize an ADC composing an MC group, a tetrapeptide composed of glycine and phenylalanine residues, and exatecan, did he?
A. He never suggested such things.
Q. The chemistry at Seagen had in 2004 wasn't suitable for linking every drug. Right?
A. It -- there's some drugs that are -- that have no functionality for conjugation.
Q. Not all drugs can be linked to antibodies using Seagen's chemistry from 2004. Right?
A. Not all drugs can be linked to antibodies, period.
Q. I'm handing you what I've marked as Exhibit 19 to your

deposition. It's a document, the first page of which has the Bates SGIEDTX00042961?

A. Yeah.

Q. Do you recognize this document?

A. Not yet. Yes, now I do.

Q. This is a presentation titled Thinking About Linking. Do you see that?

A. Uh-huh.

Q. On the -- your name is on the third slide.

A. Yep.

Q. You're -- you're listed as an associate director. You said that would have been sometime after 2010? Is that right?

A. Oh, yeah.

Q. This is later than that?

A. Yeah, I believe so.

MR. CHIVVIS: Your Honor, can we pause the video?

THE COURT: Stop the video. Stop the video, please.

MR. CHIVVIS: We request, given the way the slides are being presented here, that the courtroom be sealed for the remainder of this presentation.

THE COURT: All right. But I will say this, counsel. This is the kind of thing you all should have exchanged and discussed in advance so that we didn't have to stop this in the middle of the presentation.

But based on your request and out of an abundance of

caution to make sure anything confidential is protected, I'll order the courtroom sealed. And I'll direct those present who are not subject to the protective order to excuse themselves and remain outside until the courtroom is opened and unsealed.

Going forward, both sides need to make sure the other side knows whether there's anything potentially confidential in any of these video depositions before we get part way through them and have to stop them and interrupt the jury's concentration. I don't want that to reoccur.

(Courtroom sealed.)

(Courtroom unsealed.)

THE COURT: Ladies and gentlemen, before we proceed with the next witness, we're going to take a short recess. This is one where you may simply close your notebooks and leave them in your chairs. Please follow all my instructions about your conduct, including not to discuss the case with each other.

And we'll be back shortly to continue with the next witness from the Defendants.

The jury's excused for recess.

(Whereupon, the jury left the courtroom.)

THE COURT: Be seated, please.

Counsel, during this recess, I'm directing that you meet and confer with each other to ensure that there are not items

that are proprietary or confidential that will be displayed to the jury in any remaining deposition designations or counterdesignations to be played as a part of this trial.

I don't want this kind of interruption again. We're in the middle of the a witness' testimony, albeit by deposition, I have to stop the entire proceeding, turn the lights on, send everybody out, it's highly disruptive. There's no reason for it.

And if there's material that needs to be protected, I want to know when the deposition witness is called so I can seal the courtroom through the deposition witness' testimony. If there's not, then I want to know that, too. But this is not going to happen again. And I want you to review the designations and counterdesignations for all the remaining deposition witnesses during this recess, and then we'll proceed with the next deposition witness.

We stand in recess.

(Brief recess.)

THE COURT: Be seated, please.

Are we ready to proceed with the next witness by deposition?

MS. AINSWORTH: We are, Your Honor.

THE COURT: Are there any doubts about whether it needs to be sealed or not?

MS. AINSWORTH: It is my understanding there is no

need to seal this deposition witness or the next one.

THE COURT: All right. Then let's bring in the jury, please, Mr. Johnson.

(Whereupon, the jury entered the courtroom.)

THE COURT: Please be seated, ladies and gentlemen. Defendants, call your next witness.

MS. AINSWORTH: Thank you, Your Honor.

Defendants call by video deposition Dr. Stephen Alley, who is an executive director of scientific integration and strategy at Seagen.

The video is 6 minutes long. 3 minutes and 41 seconds are Defendant's designations, and 2 minutes, 19 seconds are Plaintiff's designations.

Doctor Alley will be talking about Defendants' Exhibits 1112.

THE COURT: All right. Proceed with this witness by deposition.

STEPHEN ALLEY, PhD., BY SWORN VIDEO DEPOSITION,

Q. And it looks like you have been working at Seagen since 2003. Is that correct?

A. That's correct.

Q. And you have a Ph.D. in organic chemistry from the University of Washington. Is that correct?

A. That's correct.

Q. And then you also have a -- did post-doctorate work at

Penn State University. Is that correct?
A. That's correct.
Q. I'm going to introduce as an exhibit Exhibit 13. Yes. When did you first see it?
A. I don't remember when I first saw it.
Q. Did Doctor Senter circulate this presentation within Seagen after the IBC conference?
A. I believe that Doctor Senter sent an email to some members of the chemistry department.
Q. So what was Seagen's first awareness or when was Seagen first aware of DS-8201?
A. As I stated before, Peter Senter and Bob Lyon viewed the Abe poster, which showed the first structure of DS-8201.
Q. And is it your testimony that they viewed the poster on December 8th, 2015?
A. From what I reviewed is it was within a few days of the conference.
Q. So was DS-8201 the first ADC you became aware of that contained a tetrapeptide with solely glycine and phenylalanine residues?
A. And here, are we talking FDA approval or --
Q. No. Just in terms of the first time you saw an ADC that was a tetrapeptide that exclusively -- or that solely had glycine and phenylalanine.
A. As a specific ADC, I believe that DS-8201 -- sorry. This

is my specific awareness of an individual ADC -- where I'm struggling with is I'm aware of the '039 Patent that describes a tetrapeptide ADC with glycine and phenylalanine.

Q. So when you became aware of DS-8201, was that the first time then that you became aware of a tetrapeptide -- or an ADC containing a tetrapeptide with glycine and phenylalanine?

A. Yes, as an ADC with exclusively glycine and phenylalanine in a tetrapeptide.

Q. And do you recall when you became aware of DS-8201?

A. Not the exact date, but it probably was in 2016.

Q. And in reviewing the '340 application for today, did you see any description or disclosure of a tetrapeptide?

A. It's described right in 684. In the first sentence it says tetrapeptide.

Q. And is a tetrapeptide that's composed of glycine and/or phenylalanine residues shown in the laboratory notebooks of any of the inventors of the '039 Patent?

A. So, once again, exclusively hydrogen and benzyl?

Q. Yes. Composed exclusively of glycine and phenylalanine residues, so, yes.

A. Okay. And in the inventors' notebooks?

Q. Correct.

A. In the -- you're asking for -- sorry. I just want to be sure I get the -- all the terms that you're asking for. A tetrapeptide drug linker composed of solely glycine and

phenylalanine in the inventors' notebooks?
Q. Yes.
A. In my review of the inventors' notebooks, I did not see a tetrapeptide that was solely composed of glycine and phenylalanine.
Q. So with any of the work that is described in the '039 Patent, and specifically in regard to intracellular cleavage, did Seagen perform any research to show intracellular cleavage or to support the intracellular cleavage that is claimed in claim 1?
A. Seagen did internal work with assays similar to the ones that I highlighted on Seattle Genetics' antibodies, and that immunologic specificity of requiring the target antigen that would cause the internalization is an example of an experiment that can be done to demonstrate intracellular cleavage.
THE COURT: Does this complete this witness by deposition?
MS. AINSWORTH: It does, Your Honor.
THE COURT: Call your next witness, please.
MS. AINSWORTH: Defendants call Dr. Robert Lyon, who is a senior director of chemistry at Seagen.
The video is 5 minutes 33 seconds long, and all of that time is Defendant's designations. And Doctor Lyon will testify with regard to Defendant's Exhibit 111.
THE COURT: Proceed with this witness by deposition,

please.

ROBERT LYON, PhD., BY SWORN VIDEO DEPOSITION,

Q. And, Doctor Lyon, how long have you been working at Seattle Genetics?

A. I started at Seagen in 2005, so about 16 years.

Q. And then you went to Seagen, it says, May 2005. Is that right?

A. That's correct.

Q. And what was your initial position at Seagen in 2005?

A. I was a scientist in the protein conjugation group.

Q. And what percentage of your work at Seagen has related to ADCs?

A. The large majority. Perhaps 90, 95 percent.

Q. Were the antibodies that were used in the DR5 collaboration with Daiichi Sankyo antibodies that were provided by Daiichi Sankyo?

A. Yes.

Q. And the drug linkers that were used in the collaboration with Daiichi Sankyo relating to DR5 were drug linkers provided by Seattle Genetics. Is that right?

A. Yes.

Q. What drug linkers were used?

A. I recall both the MC-VC-MMAE and the MC-MMAF drug linkers being used as part of that a collaboration.

Q. Do you recall ever conjugating a drug linker containing a

tetrapeptide in connection with the DR5 collaboration?
A. No.
Q. Are you aware of anyone at Seattle Genetics telling Daiichi Sankyo to use a tetrapeptide in a drug linker in an ADC?
A. No.
Q. Did all of the drug linkers that were used in the Daiichi Sankyo collaboration contain an auristatin?
A. To my knowledge, yes.
Q. We have been talking about a number of different projects that you've worked on over your 16 years at Seattle Genetics. Did any of those projects involve a drug linker containing a tetrapeptide composed of glycine and phenylalanine residues?
A. I don't recall such a drug linker.
Q. In your time at Seattle Genetics, did anyone ever provide you with a drug linker containing a tetrapeptide composed of glycine and phenylalanine residues to conjugate to an antibody?
A. Not that I recall.
Q. Did anyone ever suggest to you during your time at Seattle Genetics that a tetrapeptide composed of glycine and phenylalanine residues would be desirable for a drug linker in an ADC?
A. Not that I recall.
Q. The first time that you saw an ADC containing a

tetrapeptide composed of glycine and phenylalanine residues was in the Daiichi Sankyo HER2 ADC. Is that right?

A. As presented in a conference poster.

Q. You had never seen in any other context -- well, prior to that conference poster, you had never seen an ADC containing a tetrapeptide composed glycine and phenylalanine residues.

A. I do not recall seeing one prior to that poster.

Q. Doctor Lyon, I'm going to show you a document that's been marked as Exhibit 7.

And the first time that you can recall ever seeing a tetrapeptide composed of glycine and phenylalanine residues like the tetrapeptide used here in the drug linker in an ADC was in this poster. Right.

A. This is the poster where I have already stated that I first saw this linker structure.

Q. Okay. How many times have you discussed Daiichi Sankyo's ADCs since December 2015 with Peter Senter?

A. Specifically with Peter Senter, yeah, I don't have any. It's a difficult question to answer. What was the date you said?

Q. Since the date of --

A. In 2016?

Q. -- yeah, since December and 2015?

A. '15. So six years. I don't know. I -- that's -- I couldn't answer that.

Q. More than 10 times?
A. Probably more than 10 times.
Q. Did Peter Senter ever mention to you that he had invented the linker technology used in Daiichi Sankyo's ADC 10 years before that?
A. No, not that I recall.
THE COURT: Does that complete this witness by deposition?
MS. AINSWORTH: It does, Your Honor.
THE COURT: All right. Thank you.
Defendants, call your next witness.
MR. CHIVVIS: I just conferred with counsel about where --
THE COURT: Obviously you just conferred with counsel. Is there anything that you need to raise with me?
MR. CHIVVIS: I just noted an area if he explores that we would need to seal the courtroom. We're not aware of that area being broached at this time.
MR. RATLIFF: Not at this time, Your Honor.
THE COURT: All right. Call your next witness, please, Mr. Ratliff.
MR. RATLIFF: Your Honor, Defendants call to the stand Dr. John M. Lambert.
THE COURT: All right. Doctor Lambert, if you'd come forward and be sworn, please.

(Whereupon, the oath was administered by the Clerk.)

THE COURT: Please come around, Doctor Lambert, have a seat on the witness stand.

Mr. Ratliff, you may proceed with direct examination.

MR. RATLIFF: Thank you, Your Honor.

JOHN M. LAMBERT, PhD., SWORN,

testified on direct examination by Mr. Ratliff as follows:

Q. Doctor Lambert, would you please introduce yourself to the ladies and gentlemen of the jury?

A. My name is John Lambert. I'm a scientist and, probably as you can tell from my accent now, originally from England.

Q. Doctor Lambert, where in England are you from?

A. Well, I was born in London in 1951, and the oldest of five. My parents were from Manchester, moved back to the city of Manchester in the northwest of England when I was about five, and that's where I was brought up.

Q. And when did you come to the United States?

A. I came to the United States in 1976 to do post-doctoral research at the University of California at Davis.

Q. Doctor Lambert, are you married?

A. Yes.

Q. How did you meet your wife?

A. Well, actually I met my wife Cecelia at my time at University of California-Davis. She's from Davenport, Iowa, and had moved to California to never see winter snow again.

Unfortunately for her, we then got married -- well, I then moved to -- back to Britain. She came with me. We got married on Valentine's Day 1981. Later in 1981, I accepted a job in Boston, which unfortunately for her meant that she's now putting up with winter snow.

Q. And, Doctor Lambert, do you currently live in the Boston area?

A. Yes, I do. I live in Cambridge, Massachusetts.

Q. Doctor Lambert, is it okay if I show an article from a magazine called The Medicinemaker to you?

A. Yes, you can.

Q. Doctor Lambert, do you recognize this article?

A. I do.

Q. And are those pictures of you that we see here on this slide?

A. Yes. There's a couple of pictures of me in a lab coat, and there's some pictures of me rowing. I'm the person with the yellow hat in the four in the double.

Q. Can I turn your attention to the top right-hand portion of the article, which reads, "Pulling for a Cure: Lessons Learned with John Lambert." Do you see that?

A. Yes, I do.

Q. And next can I turn your attention to the words just underneath the title, where it says, "Over the past four decades, John Lambert has spent most of his time either on the

water or in the lab." Do you see that?
A. I do see that.
Q. And can you tell us what it means when it says you spent most of your time on the water?
A. Well, when I went -- when I -- as an undergraduate, I went to Cambridge University and took up the sport of rowing, fell in love with it, and so every morning in Boston at about 5:30, I would be on the water rowing with my teammates. I still row to this day.
Q. And, Doctor Lambert, can you tell us what it means when you said -- when it says that you spent most of your time either in the water but in the lab?
A. Yes. I was a research scientist. And after rowing in the mornings, feeling invigorated, I, would go to the lab and spend many, many hours as a -- as a biochemist working on ADCs.
Q. How did you become interested in science?
A. Ohh, I think my earliest recollections are probably around 9 or 10 or 11 when I was always interested in biology and nature. Our home became a zoo of animals that we would keep. And so I was always interested in biology.
When I went to high school, I had a really good chemistry teacher and became fascinated with chemistry. And so once I went to university, the study of biochemistry, or the biology of living things, was really what I wanted to do.

Q. And, Doctor Lambert, you mentioned that you went to a university. Do you have a slide that explains more about your education and experience?

A. I do.

Q. Let's turn there. Now, Doctor Lambert, can you tell us where you obtained your Ph.D.

A. Yes. I was an undergraduate at University of Cambridge and then stayed at Cambridge to do a Ph.D. in biochemistry.

Q. And where did you work after that?

A. So after earning the Ph.D., I did post-doctoral training for four years actually at the University of California-Davis, and then moved to Britain. And I was nearly two years at the University of Glasgow in the department of biochemistry.

Q. Now, Doctor Lambert, your slide says 40 years of researching ADCs. Can you explain that for the ladies and gentlemen of the jury?

A. Well, when I was in Glasgow, I -- my life plan at the -- when I moved to Glasgow was to become a professor of biochemistry at a university. But during my time in Glasgow, I started to think I would like to maybe apply my protein chemistry skills to actually developing drugs to help cancer patients.

And so I started to look for -- at advertisements for a biochemist to apply those skills, and I applied for a job at the end of 1981 to work at -- on a research project at the

Dana-Farber Cancer Institute at Harvard Medical School. And I was accepted for the job, and I took -- and I was able to take it up in 1982, just over 40 years ago.

Q. And, Doctor Lambert, how did you become interested in the field of ADCs?

A. Well, the project at the Dana-Farber Cancer Institute was funded by a group of investors that formed a company ImmunoGen, and the goal was to use antibodies to deliver toxic drugs to cancer cells more specifically.

Q. And, Doctor Lambert, you mentioned ImmunoGen. Can you tell us a little bit more about what is ImmunoGen?

A. So let's say ImmunoGen was formed by a group of investors in 1981 who formed this company. The initial work was seated within the Dana-Farbert Cancer Institute. Back in 1987, it was spun out to become an independent biotechnology company, and the goal was to develop ADCs. The goal of all of the research of ImmunoGen was to develop ADCs.

Q. And, Doctor Lambert, can you tell us about your positions at ImmunoGen?

A. Well, starting as a research scientist, when ImmunoGen spun out, I was a director of biochemistry, ultimately vice president of research, executive vice president of research. And from 2008 until I started the process of retirement, I was chief scientific officer. I retired from the company a little over four years ago now.

Q. And while at ImmunoGen, Doctor, were you ever involved in any programs that resulted in the an FDA-approved ADC?
A. Yes. I was very fortunate to be a -- in a research group that did develop a technology that led to an FDA-approved medicine.
Q. And do you have a slide that explains more about that?
A. I do.
Q. Let's turn to your next slide.
And, Doctor Lambert, please -- please tell us what you're describing on this slide.
A. So what I'm describing on this slide, the team at ImmunoGen developed a drug that was able to be linked to antibodies. It was called DM1. We weren't very creative with our names.
And then we -- ImmunoGen contacted GenenTech in the late 1990s to be able to attach ImmunoGen's DM1 to GenenTech's antibody that binds to HER2. That's an antibody that binds to breast cancer and, as a result of this collaboration, became the breast cancer drug Kadcyla. And it was the first ADC approved to treat a solid tumor and the first ADC approved to treat breast cancer.
Q. Now, Doctor Lambert, over the course of your career, have you been recognized in the field of ADCs?
A. I have been so fortunate, yes.
Q. And have you prepared a slide to explain?

A. Yes.
Q. Let's turn to your next slide. And, Doctor Lambert, does this describe your recognition in the field?
A. Yes. This lists a few of the awards I've -- have been fortunate enough to receive over the years.
Q. And are there any particular awards that you've obtained in the ADC field that you're proud of?
A. Well, there's a particular award that I highlight in 2016 when I won the World ADC Award for the long-standing contributions to the field. The field was ADCs.
Q. And, Doctor Lambert, are you being compensated for your work and analysis on this matter?
A. I am.
Q. And is your compensation dependent in any way on the outcome of this matter?
A. It is not.
MR. RATLIFF: Your Honor, at this time we would like to tender Doctor Lambert as a technical expert in the field of ADCs.
THE COURT: Is there objection?
MR. CHIVVIS: No objection, Your Honor.
THE COURT: Without objection, the Court will recognize this witness as an expert in that designated field.
Please continue, counsel.
Q. (BY MR. RATLIFF) Doctor Lambert, have you prepared

slides to assist with the presentation of your testimony today?

A. I have.

MR. RATLIFF: Mr. Campos, let's please bring up those slides.

Q. (BY MR. RATLIFF) Now, Doctor Lambert, would you please give us a brief overview of what you plan to testify about?

A. Well, first, I'm going to -- you've heard a lot about ADCs in the past two days. There are a few things that I want to highlight that perhaps haven't been emphasized as much.

Secondly, I'm going to discuss why I believe that Enhertu does not infringe the patent-in-suit based on my analysis of all the information.

And, thirdly, I'm going to discuss why I believe the patent-in-suit is invalid, again based on my analysis of all the information.

Q. And, Doctor Lambert, can we now talk about what you want to highlight regarding ADCs?

A. Certainly.

Q. Let's go to the next slide.

And, Doctor Lambert, what is significant that you want to explain to us about this particular slide?

A. Well, I certainly want to convey that ADCs are highly complex drugs. One thing that hasn't been -- the antibody here is shown in blue. You've seen these types of pictures

before. You've seen pictures of linker drug moiety. You've seen those type of pictures before.

One of the things I want to emphasize is that all of the chemical elements of the linker and drug moiety can all interact with each other. It's a really complicated interplay of properties. So to get an ADC that really has the -- that works and has the desired properties for injection into people is really complex.

Q. And, Doctor Lambert, at the bottom of your slide, I see the numbers DX 69, DX 77, DX 78, DX 88, DX 89, DX 183, and DX 186.

Is that information that we could turn to in those documents to explain the concepts that you just described?

A. They are.

Q. Now, Doctor Lambert, how would you describe the task of designing and creating new potential useful ADCs for new ADCs?

A. It is very difficult.

Q. And can you tell us who are some of the companies that were involved early in the field?

A. Yes. I prepared a slide to show you that.

Q. Let's go to your next slide. And what are you showing here, Doctor Lambert?

A. So what I'm showing here is some of the early innovators in the field in the 1980s. I've just said ImmunoGen was started in 1981, for example. Immunomedics at the bottom was

started in 1982. And so during the '80s is when the ADC field started.

Q. And, Doctor Lambert, are there different types of ADC linkers?

A. There are.

Q. Can we turn to your next slide?

Now, reading the title here, it says, ADCs with Cleavable Linkers. What do you mean by that?

A. Well, ADCs can have either cleavable or uncleavable linkers. The uncleavable linker is obvious. The linker cannot be cleaved. But the cleavable linkers come in two flavors.

Q. And can you talk to us and explain more about the first flavor?

A. Well, once an enzyme has cleaved the peptide, and you've heard about this, elements of the -- of the spacer, which I represent in purple here, and if you look at the top row, can be -- completely fall off spontaneously and so leave -- leave a drug moiety that has no elements of the spacer still on it. And I call that a traceless cleavable linker.

So the payload released in the cancer cell is the drug moiety without any other bits added to it.

Q. And, Doctor Lambert, does the traceless cleavable linker have any particular significance to this case?

A. Yes, it does.

Q. How?
A. The claims, the claim 1 of the '039 Patent, requires that the drug moiety be released from the linker as a tracer -- in the manner of the top image here.
Q. Now, Doctor Lambert, we see on your slide at the bottom there is a picture, and underneath it, it says non-traceless cleavable linker. Can you explain to us what you mean by this portion of the slide?
A. So if after any process of enzyme cleavage to release the drug moiety with part of the linker still attached, the purple spacer is represented here, if the spacer doesn't fall off or only partially falls off, as drawn in this thing, so the final payload in the cancer cell still has a bit of the spacer on it. It's actually a new drug, and you would call that a non-traceless cleavable linker. It's a different chemical entity.
Q. And, Doctor Lambert, does this non-traceless cleavable linker concept have any particular significance to this case?
A. Yes, it does.
Q. And can you please explain?
A. Well, Enhertu is an ADC that releases a payload that -- by this bottom mechanism, the drug moiety still has a piece of linker attached.
Q. Now, Doctor Lambert, at the bottom of your slide, I see another set of DX exhibits, DX 83, 134, 157, 166, 167, 172,

180, 190, and 199.

Is this also information that we can turn to to understand more about the concepts that you discussed on this slide?

A. Yes, they are.

Q. Now, Doctor Lambert, did early ADC research focus on the cleavable linkers?

A. Yes, they did.

Q. And can you give us a little bit more background about that?

A. Yes.

Q. So let's turn to your next slide.

And we can actually turn a little bit forward to your -- the next slide. And let's talk a little bit more about Seagen.

So can you give us some background as to Seagen as a company?

A. So Seagen was started in 1998, and it became well known for its development of monomethylvaline compounds. These compounds are drugs of the auristatin type, in particular, two of them, MMAE and MMAF, which stand for monomethylvaline auristatin E or monomethylvaline auristatin F.

Q. And, Doctor Lambert, does Enhertu contain these auristatin compounds that you're discussing?

A. No, it doesn't.

Q. And we see on this slide DX 235. Is that an exhibit that talks more about these auristatin compounds?
A. Yes, it is.
Q. Now, Doctor Lambert, can I turn your attention to a document?
MR. RATLIFF: Let's bring up DX 129.
Q. (BY MR. RATLIFF) And I think we've seen this document before.
A. Yes.
Q. And, Doctor Lambert, can you explain to us about this document? Does it have any particular significance to this case?
A. Yes. It's a document -- it's a research paper in the Nature Biotechnology authored by Doctor Senter and Doctor Sievers.
Q. And let's turn to the second page of this document starting with selecting the right drug linker. Would you please explain what's meant here on this portion of the document?
A. What's meant here is that the authors are describing the development of Seagen's ADC platform technology, and their platform technology is the use of the -- of linkable versions of auristatins, the development of these monomethylvaline compounds, or MMAE, MMAE in particular in this article.
Q. And we see here on the slide on the right, there's a

description that talks about, upon peptide cleavage, the PABC group rapidly fragments leading to the release of MMAE in chemically unmodified form.

Can you explain to us what's meant there, Doctor?

A. So what's meant there is that, upon cleavage of the linker, the PABC group, that's actually the spacer between a peptide linker and the MMAE drug, and all of that falls off so the MMAE is -- is the payload released in the cancer cell in unmodified form. It's the original MMAE.

Q. And, Doctor Lambert, are you aware of other Seagen papers like this?

A. Yes, I am.

Q. And let's turn to your next slide. And, Doctor Lambert, what are you showing here on this slide?

A. What I'm showing here is just a selection of very many publications in the scientific literature by Seagen scientists, and they all focused on antibody auristatin conjugates since the auristatins -- developing linkable versions of auristatins was their technology.

Q. And, Doctor Lambert at the bottom of the slide, we have more DX numbers, DX 164, 168, 173, 195, 221, and 246.

Are these DX numbers reflecting the articles that you are showing up here on this slide.

A. Yes, they do.

Q. Now, do any of these articles, as you're aware, discuss

tetrapeptides?
A. No.
Q. Now, Doctor Lambert, to your knowledge, has Seagen engaged in research collaborations with other companies?
A. They have.
Q. Let's turn to your next slide.
Now, I see the title of your next slide reads, Typical Seagen Collaboration Model. What do you mean by that, Doctor Lambert?
A. Well, Seagen had developed a drug that would -- was linkable to antibodies, that is, their monomethylvaline compounds of two flavors, MMAE or MMAF. They sought to partner with companies, large pharma, that had antibodies that would bind to specific cancers. And so, together, they would be able to make a medicine that the antibody would be able to provide the targeting to cancer component and Seagen's auristatin technology would provide the drug that could be delivered as an ADC to the cancer cells.
Q. And, Doctor Lambert, what are you showing on the right-hand side of the slide?
A. What I'm showing on the right side are three different linker drug chemical elements. They are all auristatin drugs, either MMAE or MMAF, linked to either a cleavable or an uncleavable linker.
Q. Doctor Lambert, do any of these drug linkers contain a

tetrapeptide?
A. They do not.
Q. And do any of these drug linkers contain a tetrapeptide with only G and F?
A. They do not.
Q. And what are you explaining on the left-hand side of the slide?
A. So on the left-hand side is -- is just pointing out that the antibody component of the ADC in these partnerships was provided by the partner. ImmunoGen itself, the company I worked for, also did this type of partnership as I showed you earlier. The drug Kadcyla was developed by one of these partnerships. ImmunoGen developed a DM1 drug. GenenTech had an antibody that bound breast cancer. Together, we made a drug.
Q. Does Seagen have FDA-approved ADCs?
A. Yes, it does.
Q. And can we turn to your next slide?
Now, Doctor Lambert, what are you trying to convey on this particular slide?
A. What I'm conveying here is that Seagen's FDA-approved ADCs with a cleavable linker, there are four of them and not the same as Enhertu.
Q. And what do you have in the various columns?
A. So in the various -- so there are many differences

between Enhertu and the Seagen FDA-approved ADCs. I just highlight some of the ones that are perhaps pertinent to the discussion or evaluation here.

Q. And so, Doctor Lambert, can you tell us how we are to explain or how you are referring to the X's and the checks?

A. Yes. So the first item there is that the cleavably -- do the cleavable ADCs, the first question, do they release the free or modified drug or not? Enhertu does not.

Therefore, Seagen-approved ADCs with cleavable links release free MMAE, or a free drug, without any part of the linker attached.

Q. And, Doctor Lambert, at the bottom I see the DX exhibits 57, 58, 59, 60, 64, 225, 236.

Are these references to explain the concepts that you're showing on this slide?

A. They are.

Q. Now, can we take a look at the patent-in-suit, Doctor?

A. Yes.

MR. RATLIFF: Let's bring up DX 1.

Q. (BY MR. RATLIFF) And I'd like to turn your attention, Doctor, to the first page of the patent and looking at the title of the patent.

And, Doctor Lambert, you spoke to us earlier about monomethylvaline compounds. Can you remind us what they are?

A. So the monomethylvaline compounds are the auristatins

developed by Seagen, linkable versions of auristatin.
Q. And does the title of the patent give a description regarding monomethylvaline compounds?
A. Yes. It describes monomethylvaline compounds that are capable of conjugation or joining to an antibody or to a ligand, but an antibody can be a ligand.
Q. And, Doctor Lambert, let's take a look at the first page of the patent, and I want to turn your attention to the abstract.
What does the abstract tell us about the patent-in-suit?
A. Well, the abstract of a document is always a brief description of what the document's about, and as you can see, the document's about auristatin peptides that are MMAE and MMAF.
Q. Thank you, Doctor.
And if we zoom back out, does the title -- does the front page of the patent also talk about when it was filed?
A. Yes, it does.
Q. And can you tell us what is the filing date for this patent?
A. The filing date was July 2019.
Q. Now, Doctor, by this date had Daiichi Sankyo already applied for its own patents covering Enhertu?
A. Yes.
MR. RATLIFF: Let's take a look at DX 691.

Q. (BY MR. RATLIFF) Doctor Lambert, do you recognize this document?
A. I do.
Q. And what is it?
A. It's a United States patent describing an antibody-drug conjugate, and the applicant is Daiichi Sankyo company.
Q. And does this patent cover Enhertu?
A. It does.
Q. And when did it issue?
A. It issued in November 7th, 2017.
Q. And, Doctor Lambert, let's take a look at DX 692. Do you recognize this document?
A. I do.
Q. What is it?
A. It's another patent that issued from this filing about antibody-drug conjugates, and the applicant was Daiichi Sankyo company.
Q. And does it also cover Enhertu?
A. It does cover Enhertu.
Q. And when did -- when was this patent granted by the United States Patent Office?
A. It was granted on February the 5th, 2019.
Q. And can you remind us, is that before or after Seagen applied for the patent-in-suit?
A. It's nearly six months beforehand.

Q. Now, Doctor, can we take a look at DX 693?
Do you recognize this document?
A. I do.
Q. What is it?
A. It's another patent from the series describing specifically now an antiHER2 antibody-drug conjugate.
Q. And does this patent cover Enhertu?
A. It does cover Enhertu.
Q. And when did the United States Patent Office grant Daiichi Sankyo this patent?
A. On December 18th, 2018.
Q. Thank you, Doctor.
Now let's take a look again at Seagen's 2019 filed patent, so let's bring up the first page of DX 1.
Q. (BY MR. RATLIFF) Now, Doctor Lambert, does this patent tell us anything about the first application that was filed with the United States Patent Office?
A. Yes, it does.
Q. And can I turn your attention to the related U.S. application data?
A. Yes.
Q. And does this portion tell us anything about the original application of Seagen's patent?
A. Yes. If you start at the bottom, it tells you when the very first filing of this patent application was filed, and it

was on November 5th, 2004.

Q. And, Doctor Lambert, what was the patent number for that first application?

A. The patent number was 7,498,298 or, in short, '298.

Q. And can I show you a document that's been marked as DX 2?

A. Yes.

Q. And do you recognize this?

A. I do. It's that patent, '298.

Q. And is this patent identical in terms of its specification to the 2019 filed Seagen patent?

A. Yes. All just over 200 pages of the patent document are identical.

Q. And, Doctor Lambert, can you give us an overview of what's claimed in this patent?

A. Certainly.

MR. RATLIFF: So we can turn to the back end portion of the patent, and we can blow up the claims.

Q. (BY MR. RATLIFF) So, Doctor Lambert, can you tell us, does this patent claim any ADC linkers at all?

A. No. This patent claims no linkers.

Q. And so what does this patent claim?

A. The patent claims a compound, a chemical with the following general structure, and that's the picture. And that linear structure is the core structure of an auristatin-type drug.

Q. Thank you, Doctor.

Now, if we can turn to your slides, slide 14.

Now, Doctor Lambert, can you please give us an overview as to why you believe Enhertu does not infringe the '039 patent?

A. So the first point is that claim 1 has certain structural and functional requirements, and Enhertu does not meet them.

Q. And I see a second bullet on this slide. Can you please explain this bullet?

A. Well, claim 2 requires a self-immolative spacer, and Enhertu does not have a self-immolative spacer as defined in the claim.

Q. Now, can you -- do you have a slide that explains more about your first reason why Enhertu does not infringe the '039 Patent?

A. I do. I do.

Q. Let's turn to your next slide.

And we're looking here at the title says Claim 1 Requires the Drug Moiety to be Intracellularly Cleaved.

Can you explain to us what is meant by this, Doctor?

A. So what is required here is the drug moiety must be cleaved intracellularly in the cancer cell to release the unmodified drug.

Q. And can you explain what is meant by releasing this unmodified drug?

A. What is meant is that the unmodified drug moiety is the payload released in the cancer cell.

Q. Now, Doctor Lambert, in doing your analysis, did you apply the Court's construction?

A. I did.

Q. And let's turn to your next slide.

And can you -- I see in this slide you have highlighted on the right 'free drug'.

A. Yes.

Q. Why did you highlight 'free drug'?

A. Because the Court's construction intracellularly cleaved results in free drug. And by free drug, that means the drug without any elements of the linker still attached.

Q. Now, Doctor Lambert, I'd like to turn your attention back to DX 1, which is the patent, and let's look at column 159, lines 9 through 15.

Does this portion of the patent explain anything about the free drug that you mentioned?

A. Yes.

Q. And what does it explain, Doctor?

A. Well, what it explains is that in the specification of the patent, it was contemplated --

MR. CHIVVIS: Your Honor --

THE COURT: Just a moment.

Yes, counsel?

MR. CHIVVIS: Objection. The Court has construed this term.

THE COURT: Speak up, counsel.

MR. CHIVVIS: Your Honor, the Court has construed this term. If the witness would like to talk about how the plain and ordinary meaning should be understood for the surrounding language as known in the art, that would be fine. But to go back to the patent and try to go through the specification and re-interpret the claim term, we think is inappropriate, Your Honor.

MR. RATLIFF: Your Honor --

THE COURT: What is your response?

MR. RATLIFF: Your Honor, this is not a --

THE COURT: Just a minute. What is your response, Mr. Ratliff? Wait until I call on you. Now, give it to me.

MR. RATLIFF: Your Honor, this is not a reinterpretation of the claim. We just simply asked Doctor Lambert to explain where he sees this concept from the Court's construction in the patent.

THE COURT: Well, not only is the jury but each of the witnesses and counsel are bound by the Court's constructions of any claim language that's previously been taken up.

I don't know that I view this as a direct contradiction of the Court's claim construction, and I'm going to overrule

the objection.

But I'm going to caution everybody that the Court's adopted constructions regarding any claim language must be respected and must be followed and should not be contradicted, either directly or indirectly.

But with that, you may continue your examination.

MR. RATLIFF: Thank you, Your Honor.

Q. (BY MR. RATLIFF) Now, Doctor Lambert, what does this portion of the patent explain? And we're at column 159, lines 9 through 15.

A. What it explains is that at the tumor cell, a cleavage process could result in a drug, or it could result -- it also contemplates that a drug linker compound could be released.

Q. And, Doctor Lambert, have Seagen scientists also written about this requirement of releasing free drug?

A. Yes, they have.

Q. And let's -- let me turn your attention to DX 163.

And do you recognize this document?

A. Yes, I do.

Q. And can we turn to page 3 of the document?

A. Yes.

Q. And can you explain to us, Doctor, what this portion of page 3 is describing?

A. What this portion of page 3 is describing, that if the parent drug contains vestiges of the linker, in this case a

bound peptide, it may have impaired cytotoxicity. It's a new molecule. It may not function the same way with an extra element to it.

And so it further goes on to describe the self-immolative spacer that, in the view of this paper, in a desirable way released free drug without any elements of the spacer.

Q. And, Doctor Lambert, let's turn back to your slide, which is slide 16.

A. Uh-huh.

Q. And, first of all, do you and Doctor Bertozzi agree about what part is the drug moiety in Enhertu?

A. Can you repeat the question?

Q. Yes. Do you and Doctor Bertozzi agree about what part is the drug moiety in Enhertu?

A. No, we disagree.

Q. Well, let's turn to your next slide. And what are you showing on this slide, Doctor?

A. This is the picture of Enhertu.

Q. And does Enhertu have various components that you've depicted?

A. Yes. It has various components, and I will highlight them in color so they are distinguishable.

Q. And what, in your view, Doctor, is the drug moiety in Enhertu?

A. The drug moiety is the brown chemical structure on the

far right. There is DX-8951.
Q. And, Doctor Lambert, are the DX numbers at the bottom, DX 107, 108, 109, 126, and 281, documents that inform your analysis?
A. Yes, they are.
Q. Now, have you seen internal documents from Daiichi Sankyo that make plain to you what is the drug moiety in Enhertu?
A. Yes, I have.
Q. Well, let's turn to your next slide.
Now, let's -- can you explain what you're showing on this slide?
A. What I'm showing on this slide are snapshots taken from Doctor Naito's notebook.
Q. And so this is -- is this internal work of Daiichi Sankyo?
A. It is internal work of Daiichi Sankyo where Doctor Naito synthesized for the first time the linker drug that is the linker drug of Enhertu.
Q. And how does it inform your analysis as to what is the drug moiety in Enhertu?
A. This was just one of a number of studies that Doctor Naito did where he was trying to link DX-8951 to a glycine phenylalanine only tetrapeptide using a whole variety of different spacers to actually connect them.
Q. And, Doctor, are the DX numbers at the bottom, 114, 940,

and 941, references that we can go to for the information that you looked at on this slide?

A. Yes, they are.

Q. Now, can I turn your attention to a document that's marked DX 115? Doctor Lambert, have you seen this before?

A. I have.

Q. And what is it?

A. It's a presentation made by Doctor Abe at the meeting of the Japanese Cancer Association.

Q. And let me turn your attention to slide 8 of this document.

Now, what's depicted at the top-hand portion of this slide, Doctor?

A. What's depicted at the top of the slide is that an antiHER2 antibody shown as the blue Y with a gly-gly-phe-gly tetrapeptide peptide as part of the linker connected to the exatecan, or DX 8591 -- 8951, sorry, with X through a connector that is just labeled X. X isn't a chemical compound. It's meant to represent a whole series of molecules.

Q. And what is to the right of the X?

A. To the right of the X is the drug moiety DX-8591 [sic] also known as exatecan.

Q. And so, Doctor, how does this inform your analysis as to what is the drug moiety in Enhertu?

A. How it informs me is that the Daiichi Sankyo scientists were seeking to attach DX-8951, or exatecan, to an antibody and they were exploring all the different possibilities that the linker between the drug moiety and the antibody should be in order to achieve an ADC that works.

Q. And, Doctor Lambert, can we put this slide side by side with one of your earlier slides? Maybe slide --

A. Certainly.

Q. -- slide 17? And can you explain to us where in the slide 8 is the drug moiety that we see in brown on the left-hand portion of your slide?

A. So the structure on the right shows that the drug moiety in brown, and you've seen this picture several times. The structure on the -- on the right, the far right chemical image, it's tilted on its side, but it's exactly the same chemical structure.

Q. And so, Doctor Lambert, let's just focus our attention on DX 115, again looking at slide 8.

Does this research work that we're looking at, this slide, tell us anything about the complexity of ADCs?

A. Yes, it does.

Q. Could you please explain?

A. It explains how difficult it is to actually make an ADC with the -- that it would work.

Q. And how do -- how are we to understand this slide, the

entries and what we see across the top for entry X DAR aggregate in KPL 4 IC 50?

A. Yeah. So under entry in this experimental series, that the Daiichi Sankyo scientists made seven different variations of linking the exatecan to the antibody. And what varied was the X. They used several -- several different chemicals or atoms, if you like, and, yes, different spacers.

What is DAR, as you've heard before, is the drug-to-antibody ratio or, in short, the number of drugs that you can link to one antibody.

What is aggregate is actually whether the actually ADC that you make tends to clump together. And often adding drugs to antibodies, drugs tend to have properties that sometimes make antibodies clump together. And, of course, clumping together precipitating is not a property of a pharmaceutical agent designated for injection into -- for intravenous injection.

The very far end, KPL-4, is just the name of a cancer cell line that is growing in cultures, in dishes. And it's essentially a test cell line.

And what IC 50 means, it's the inhibitory concentration that would kill 50 percent of the cells.

And the units are nanomolar, which is very low concentration.

Q. Now, Doctor Lambert, are any of these entries -- have

anything to do with Enhertu?
A. Yes. Entry 7 at the bottom, the chemical structure there that is depicted as X is -- in fact then defines the chemical structure of Enhertu.
Q. And, Doctor Lambert, on this issue of whether Enhertu infringes Seagen's 2019 filed patent, have you prepared an animation to explain how Enhertu functions?
A. I have.
Q. Let's turn to your slide 20.
And, Doctor Lambert, can you please walk us through this animation?
A. So upon arriving at a cell, an enzyme can clip the GGFG peptide from the drug moiety spacer at that particular chemical bond. The enzyme, as you've seen in previous testimony, can be represented by scissors. It cuts the bond.
Q. And then what happens next, Doctor Lambert?
A. So that molecule is released inside the cell, but it's unstable, and spontaneously half -- the end bit of it falls off, the end bit of the spacer, which leaves now a drug with part of the spacer still attached. And that can be described as being the payload delivered to the cancer cell.
Q. And, Doctor Lambert, can we turn to your next slide?
And I see it says here, Enhertu does not release free drug. What are you showing on the left-hand portion of the slide?

A. So what I'm showing on the left-hand portion is DX-8951, or exatecan, which Daiichi Pharmaceuticals had in 1994. In fact, they even tested it in the clinic, and unfortunately it didn't have a good enough therapeutic window. It was too toxic to be used on its own.

But that is the drug that then Daiichi Sankyo scientists decided to try to link this drug to an antibody in order to deliver it in a more specific way.

Q. And what are you showing on the right-hand portion of the slide?

A. On the right-hand portion of the slide then is the payload is released inside cancer cells when cancer cells have been treated with Enhertu. And you can see it's the drug exatecan, but with part of the spacer still attached.

So DXd, it's a derivative of the original exatecan. It has part of the spacer on. It does make a new molecule.

Q. And so, Doctor Lambert, on the issue of non-infringement, is there a key point we should remember on this slide?

A. The key point you should remember is that what the payload that is released at cancer cells by Enhertu is exatecan or DX-8951 with part of the spacer still attached.

Q. Now, Doctor Lambert, did you hear Doctor Bertozzi during her testimony refer to certain documents regarding DXd?

A. I did.

Q. Let's pull up PDX 3.74.

And is this one of the slides you recall seeing during Doctor Bertozzi's presentation?

A. I do.

Q. And do you agree this supports Doctor Bertozzi's opinion regarding the question of infringement?

A. No, I don't.

Q. And why not, Doctor?

A. So this slide here shows conference presentations made by safety pharmacologists or parts of FDA submissions. The focus of what safety pharmacologists are are what is -- when a patient is administered an ADC, the focus is what is free, what -- when the drug falls off, what is it? What does it do? Because if the drug falls off the antibody, it could cause toxicity. So that is actually their focus.

So the word 'free drug' in this context is in the context of a safety pharmacologist, is just what becomes free after administering an ADC to a person, for example.

Q. And, Doctor Lambert, do you have an opinion on whether or not the context in which free drug was mentioned or any drug was mentioned, does it relate to the '039 Patent?

A. I think the context of the use of words is very important.

Q. And why is that?

A. So the '039 Patent defines free drug moiety in a very specific way.

Q. And is that the way it defines drug moiety any relation to the references that we saw from Doctor Bertozzi?
A. I don't believe so.
Q. Now, can we go back to your slides, Doctor?
MR. CHIVVIS: Your Honor, objection, again, to the last Q and A about the '039 defining drug moiety a very specific way unless it was in reference to the Court's claim construction.
THE COURT: Your objection is untimely. We're not going to go back and talk about exchanges that have already taken place. Overruled.
Let's move on.
Q. (BY MR. RATLIFF) And, Doctor Lambert, looking at this slide, I just want to turn your attention to DX 64, 109, 110, and 281.
Are these references that the jury could look at to understand the concepts better that you discussed?
A. Yes, they are.
Q. Now, let's turn to your slide 25.
Now at the top of your slide 25, it reads, "Enhertu is a unique ADC." Can you explain what you mean by that, Doctor?
A. So, yes. Enhertu is a -- it is a drug that treats breast cancer and gastric cancer with amazing activity. It's a drug that does -- and it differs from -- from many of the other drugs that are -- for example, Seagen's ADCs with cleavable

links, in that the released drug at cancer cells is not the same as the drug that was attached. It still has a bit of the spacer attached.

Q. And so you show -- I see Enhertu here on the left.

A. Yes.

Q. And what comparisons are you making to the Seagen cleavable ADCs?

A. So I'm making the comparison about whether any of these ADCs release free drug in unmodified form or not. Enhertu does not. The four Seagen ADCs, all of which are good drugs, release MMAE, which is the drug moiety in unmodified form.

Q. Now, Doctor, can we talk about your opinion on non-infringement of claim 2?

A. Yes.

Q. And do you have a slide to explain that?

A. I do have a slide that I hope explains that.

Q. So let's turn to your next slide. And your next slide, please.

Now, Doctor Lambert, in doing your analysis, did you apply the Court's claim construction?

A. I did apply the Court's claim construction.

Q. And can you tell us about this requirement of a self-immolative spacer?

A. So the Court's claim construction is that the self-immolative spacer Y spontaneously degrades to release the

drug.

Q. Now, can we turn to your next slide, Doctor?

And what are you showing at the top-hand portion of this slide?

A. What I'm showing in the top portion of this slide is exactly that--a self-immolative spacer that breaks down to release the drug. The drug now is just represented by a brown ball, but it releases the unmodified drug.

Q. And this picture at the top, does it have any significance to this case?

A. Its significance is that claim 1 of the patent-in-suit requires that cleavage.

Q. And, Doctor, just I want to ask this a little differently. Is the self-immolative spacer a part of claim 1 or claim 2?

A. Oh, excuse me. Yes. Actually claim 2 of the patent-in-suit absolutely requires a self-immolative spacer that breaks down to release free drug.

Q. And what are you showing on the bottom-hand portion of this slide?

A. What I'm showing on the bottom portion is what happens with Enhertu when the spacer only partially breaks down and so the payload released in the cancer cells is the drug moiety still with a bit of the spacer attached, which is a new chemical drug.

Q. And so, Doctor, on this issue of whether or not Enhertu infringes, what is the key point and takeaway from this slide?
A. The key point is that Enhertu does not infringe because all elements of the spacer is only partially removed and the payload that is released in the cancer cell still has a bit of the spacer attached.

THE COURT: Counsel, approach the bench, please.

(The following was had outside the hearing of the jury.)

THE COURT: In looking at the Court's claim construction again wherein Y is a self-immolative spacer, the construction clearly says, where Y is a spacer that spontaneously degrades to release the drug. And it appears that the dispute that has been brewing here is that the expert is now telling the jury that to degrade to release the drug means it has to completely break down.

I'm sure the Plaintiff's view will be that it only has to degrade to the extent necessary to release the drug. That can be addressed on cross-examination, and I assume it can be addressed to the extent it's within his report on the rebuttal of your technical witness.

But I'm not going to get into claim construction disputes. And a disagreement as to whether degrades to release means degrades completely or degrades only enough to release the drug so that it's free-floating is not a

contradiction of the claim construction. And I think an argument between you two in front of the jury about claim construction is not productive.

But that doesn't mean, Mr. Chivvis, that you can't address this line of argument in both cross and rebuttal and be within the same free space or adequate room to navigate as Mr. Ratliff is with the witness on direct. Is that clear?

MR. CHIVVIS: Thank you, Your Honor. I'll take the Court's guidance on that.

MR. RATLIFF: Thank you, Your Honor.

THE COURT: All right.

(The following was had in the presence and hearing of the jury.)

THE COURT: Let's proceed.

Q. (BY MR. RATLIFF) Now, Doctor Lambert, on the issue of non-infringement of the other asserted claims, do you have an opinion?

A. Yes, I do.

Q. And what is your opinion?

A. If claim 1 and claim 2 are not met, then the other asserted claims are not met, either. They all depend on claim 1 or 2.

Q. Now, Doctor Lambert, do you recall hearing from Doctor Bertozzi about Daiichi Sankyo's prior research collaboration with Seagen?

A. I did.
Q. And do you have any thoughts on whether Daiichi Sankyo's prior research collaboration with Seagen is pertinent to the issues in this case?
A. I do.
Q. Would you please tell us your thoughts?
A. I think they're not relevant at all because their collaboration was to develop an entirely different drug that had a different antibody, different linker, different payload, entirely different. I don't see the relevance in any way.
Q. And, Doctor Lambert, did you review information regarding that collaboration?
A. I did.
Q. Now, have you prepared slides to explain your analysis?
A. I have some slides, yes.
Q. So let's turn to your next slide.
Now, Doctor, can you please explain why you believe the information exchange is not relevant to the questions of non-infringement in this case?
A. Well, first, I think the exchange of information is standard and expected between two companies trying to develop a product. And, indeed, my own experience at ImmunoGen, we've had many such collaborations to try to develop products. One of them became a product. This is just the normal interchange of scientists working on such a project.

Q. And, Doctor Lambert, at the bottom of your slide, it reads, "Collaboration was limited to a specific antibody and monomethylvaline compounds." What do you mean by that?
A. Yes. The collaboration was designed to make an ADC that had a particular antibody and to link to them a set of monomethylvaline compounds, specifically MMAE and MMAF.
Q. And, Doctor Lambert, does Enhertu contain a monomethylvaline compound?
A. No, it does not.
Q. Can we turn to your next slide?
Now, Doctor Lambert, I want to ask you first, during your time at ImmunoGen, were you ever involved in research collaborations with other companies?
A. Yes, many.
Q. And was that a common thing to do at an ADC company?
A. Yes. It was common for a small biotech that had developed a technology, for example, a payload that could work as an ADC, to then seek collaborations with other companies, especially large pharmaceutical companies, that may have got antibodies that would bind to particular cancers, so that together you could make a product, a medicine.
Q. And was it also common to have your own internal program?
A. Yes. At ImmunoGen, we ran five or six external collaborations simultaneously as well as continuing our own work to develop our internal programs.

Q. Now, Doctor Lambert, the title of your slide reads, "The 2008 Daiichi Sankyo-Seagen collaboration focused on monomethylvaline ADCs." Can you explain to us what you're indicating on this slide?
A. I'm indicating that the collaboration focused on Seattle Genetics' monomethylvaline compounds as a drug moiety, and Daiichi Sankyo provided an antibody that bound to a particular target found on cancer cells.
Q. And it also talks about on this slide, "Seagen provided research and development support for specific ADCs." Do you see that?
A. Yes.
Q. And can you explain what you mean by that bullet?
A. Well, in the course of Daiichi Sankyo and Seagen making specific ADCs, Seagen would provide research support and development for its -- its expertise in monomethylvaline compounds and the linker.
Q. And is anything about the interactions between the parties untypical from what you've observed?
A. Not at all. The bottom bullet, it was very common for then the large pharma to do all the preclinical studies to evaluate the compound.
Q. And can we turn to your next slide?
And, Doctor, I believe we might have seen at least a depiction on this slide before, but can you tell us what we're

looking at?
A. What we're looking at, in the course of the collaboration, that five different -- three different ADCs were made from Daiichi Sankyo's anti-DR5 antibody, with either MMAF or MMAE, the two auristatins that are monomethylvaline compounds.
Q. And of these collaboration compounds, do any of them contain a tetrapeptide in the ADC?
A. No.
Q. Now, Doctor Lambert let's take a look at your next slide.
And I see here a picture on the right. Can you explain to us what you're showing?
A. On the right again is the chemical structure of Enhertu.
Q. And what do you have here on the left?
A. And on the left are the three collaboration compounds that were developed during the collaboration between Daiichi and Seagen.
Q. And the title of your slide reads, "The collaboration ADCs were very different." Can you explain to the jury why they were different, in your opinion?
A. Well, they're very -- they have a different antibody, a different linker, and a different drug moiety, so they're different in every way.
Q. And, Doctor Lambert, I notice, as we're looking at the slide, it's flat. But if we were able to actually see the

materials on the left and the material on the right, can you give us an insight as to what it may look like?

A. I'm not sure if I understand your question.

Q. Well, Doctor Lambert, are the ADCs that are depicted here, is this a depiction in the 2D space?

A. Yes, I understand. Yes, these chemical drawings are often done on a flat piece of paper, but you have to think the atoms all fold up and create complex shapes. And so the shape of the -- of the linker drug moiety of -- of Enhertu will be a completely different shape and structural properties in it are three dimensions than the auristatin peptides with the -- with the linkers used on those -- in those structures.

Q. And, Doctor Lambert, do you recall what were the leading or most promising ADCs in the collaboration between Daiichi Sankyo and Seagen?

A. Yes. I have read that.

Q. And are the lead ADCs depicted on this slide?

A. So the lead ADC is the top one.

Q. And, Doctor Lambert, does that top lead ADC, does it have a cleavable linker?

A. No, it does not.

Q. And is that of any significance to this case?

A. Yes, it is, because the lead ADC that was -- on which a lot of work was spent to develop it, in order to take it to the clinic, you heard the decision was in the end it didn't

go, but all of that work was about linking an auristatin drug moiety to a -- to an antibody with an uncleavable link.

Q. And, Doctor Lambert, do you have a slide that explains how different the lead ADCs were in the collaboration compared to Enhertu?

A. Yes, I do.

Q. Can we take a look at your next slide?

And, Doctor Lambert can you explain to us what we're seeing here on this slide?

A. So this summarizes some of the things we've been saying. First, the antibody is a completely different antibody, and I know from experience that different antibodies behave differently in manufacturing. The lead collaboration ADC has no peptide sequence in the linker whereas Enhertu has a tetrapeptide.

Q. And I see here, Doctor, you have in the line, cleavable linker.

A. Yes.

Q. And what's this a reference to?

A. So the lead collaboration ADC, the linker does not cleave at all, whereas in Enhertu it is a cleavable linker.

Q. And, Doctor Lambert, can you please explain to us the last two rows on this slide?

A. So the lead collaboration ADC had a monomethylvaline compound, specifically the compound MMAF, and the DAR value

was in the range of 2 to 4 drugs linked per antibody molecule, whereas the Enhertu has a camptothecin, or DX-8951, and the DAR value is around 8 drugs were linked per antibody.

Q. Now, Doctor Lambert, I'd like to show you a document that was used by Doctor Bertozzi. It's one of Doctor Bertozzi's exhibits. So let's bring up PDX 3.93.

And you see here, Doctor, on the right-hand portion of the slide --

A. Yes.

Q. -- it refers to manufacturing process. Do you see that?

A. I do see that.

Q. And do you have an opinion on Doctor Bertozzi's discussion of manufacturing in conjugation processes?

A. I do.

Q. And can you explain are manufacturing in conjugation processes at all pertinent to the claims in this patent-in-suit?

A. They are not.

Q. And do you have a slide explaining your opinion?

A. I do have a slide to show that, yes.

Q. Let's turn to your next slide.

Now, at the top here, Doctor, you write, "Seagen's patent does not claim any manufacturing process." What do you mean by that?

A. What I mean by that is that what is claimed in the '039

Patent, claim 1, has no recipe to manufacture an ADC at all. There are no conditions of temperature or other reaction conditions are included and stated which you would have in a manufacturing patent. None of the chemical substances used to perform the manufacturing are even indicated. So actually all of the manufacturing is not relevant at all to claim 1.

Q. Now, in your review of information for this case, did you review information regarding how Enhertu is manufactured?

A. I did.

Q. And did those documents set out the manufacturing process?

A. Yes, they summarized the process.

Q. And so I'd like to bring up a modification of Doctor Bertozzi's slide that she showed earlier.

And, Doctor Lambert, you see here that Doctor Bertozzi used this slide but without the X. Do you recall that?

A. I do recall that.

Q. And can you please tell us what you're showing here with the X on the slide?

A. What I'm showing here is that the manufacturing processes for Enhertu, which has a different antibody, a different linker, and different drug moiety, are entirely different from the manufacturing processes of the collaboration project, and so there is no direct connection between the information that was needed to manufacture the collaboration project and

Enhertu.

Q. And, Doctor Lambert, do you have a slide in table format to help --

A. I do. I do.

Q. So let's turn to your next slide.

And would you please tell us what you're trying to convey in this slide?

A. What I'm trying to convey here is what parts of making an ADC were actually well-established in the field and well-known in the art, and when -- and by when these operations were known in the public domain.

Q. And, Doctor Lambert, we see here in the first row, it's a mention of cysteine conjugation. Do you see that?

A. I do.

Q. And what are you explaining with the checkmarks?

A. So cysteine conjugation to antibodies was known in the 1980s. There's a CytoGen patent that was issued in 1989. And Daiichi Sankyo were using it, but it was, you know, much later.

Q. And can you remind us, Doctor Lambert, were the use of Daiichi Sankyo with cysteine conjugation in the CytoGen patent all prior to any collaboration with Seagen?

A. Yes. In fact, the CytoGen patent was well before Seagen even existed as a company.

Q. Now, Doctor Lambert, if I can turn your attention to the

other parameters that are shown in your slide, underneath cysteine conjugation, are these parameters that Doctor Bertozzi talked about in her presentation?

A. They are.

Q. And can you explain to us what you're showing on your slide with respect to those parameters?

A. What I'm showing on the slide is that, for example, use of EDTA as a chelating agent and use of NAC as a quenching agent, if you look on the far right, I mean, these were of general use in protein chemistry at the time. I mean, I remember using EDTA as an undergraduate even.

Q. And, Doctor, I see at the bottom of your slide some additional DX numbers--DX 124, 125, 159, 223, 226, 233, 237, 247, and 251. Are these materials that you looked at to prepare this slide?

A. They are.

Q. Now, Doctor Lambert, if we can turn to your next slide.

And at the top, your title reads, "Seagen did not invent cysteine conjugation with an MC group." Can you explain to us what is depicted in the top-hand portion of the slide?

A. Yes. So what I'm simply showing is that the use of antibodies to make ADCs, the use of a stretch or attachment unit to cysteine residues, the use of linkers and use of drug moieties all existed in the art.

Q. And, Doctor Lambert, what are you showing with respect to

CytoGen on the left?
A. So with respect to CytoGen, that is the issued patent dated 1989 which was making ADCs using cysteine conjugation.
Q. And what are you showing with respect to NeoRx on the right?
A. NeoRX, which is another biotechnology company, had an issued patent in 1991 where they specifically used the MC linker unit to react with those cysteine residues.
Q. And, Doctor Lambert, in your review of materials for this case, did you see any work from Daiichi Sankyo prior to any collaboration with Seagen that were using these basic protein chemistry techniques?
A. Yes.
Q. Can we turn your next slide?
And the title reads, "Daiichi Sankyo was using an MC unit before its collaboration with Seagen." Do you see that?
A. I do.
Q. And can you explain to us what you're showing on this slide?
A. These are just snapshots of various pages from notebooks at Daiichi Sankyo which showed that they were using the MC unit to make ADCs well before the collaboration even started.
Q. And, Doctor Lambert, when you had an opportunity to review Daiichi Sankyo's internal work before any Seagen collaboration, what was your impression of Daiichi Sankyo's

research?
A. Well, I actually -- when I looked at the work that they were doing in the -- as early as 2003--I was not knowing that Daiichi Sankyo was working on ADCs at that time--I was impressed by the work that they were doing and, indeed, I thought that if they perhaps knew more about AD -- linking drugs, linkers to antibodies than even ImmunoGen's research of the, say, 1999 to 2002 period. I was actually quite impressed with what they were doing.

Now, of course, big pharma doesn't really publish its -- what it's working on, unlike little biotechs that always have to publish to keep their -- keep funding -- keep excitement in the venture capital community, for example.

Q. And, Doctor Lambert, do you recall hearing Doctor Bertozzi's testimony where she said that Seagen validated the use of MC and cysteine conjugation in ADCs?

A. I did hear that.

Q. And do you agree?

A. I disagree with that.

Q. Why do you disagree?

A. I disagree because cysteine conjugation and the use of MC linker was already publicly known in the public domain at the time. What Seagen validated was the use of their monomethyl auristatin compounds as good drugs to be able to link to antibodies.

Q. And, Doctor Lambert, do you recall Doctor Bertozzi testifying about certain laboratory notebooks of Daiichi Sankyo scientists?
A. I do.
Q. And do you recall Doctor Bertozzi referencing the use of, quote, SG-type?
A. I do.
Q. And do you have an understanding of what -- or do you have an opinion about what reference to SG-type meant?
A. Yes, I do.
Q. And do you have a slide that explains that?
A. And I have a slide that shows that.
Q. Let's turn to your next slide.
So can you explain to us what you're trying to convey on this slide?
A. What I'm trying to convey on this slide is that in the relevant time frame there were two companies that were developing ADCs with payloads that looked promising. One was Seagen with the auristatin payloads, and one was ImmunoGen with its DM1 payload that I've referred to before.
Q. And, Doctor Lambert, you were working at ImmunoGen. Correct?
A. I was.
Q. And so are the references to SG-type in the laboratory notebooks, were they surprising for you to see?

A. They were not surprising for me to see because in my conversations with other scientists, especially other companies that ImmunoGen was trying to collaborate with, I would often use the word Seattle Genetics-type conjugation to describe the conjugation through cysteines as distinct from ImmuneGen-type conjugation, which was at different amino acids; it was a different chemistry.

Q. And, Doctor Lambert, at the bottom of the slide I see a reference to DX 92, DX 250, and DX 252.

Are these references that the jury could look at to understand more about cysteine conjugation and lysine conjugation?

A. Yes, they are.

Q. Now, Doctor Lambert, can we turn to your next slide?

A. Yes.

Q. Now, the title of your slide is, "Daiichi Sankyo's work on Enhertu before issuance of the '039 Patent." Why did you prepare this timeline?

A. I prepared this timeline because the -- to represent the time gap between the filing of the original Seagen patent application and the filing of the '039 Patent.

Q. And so can we walk through this timeline?

A. Certainly, yes.

Q. And so what is the first date that's depicted here on the left?

A. So on the left November 5th, 2004, is when the first -- the application was filed that contains all of the specifications of the patent.

Q. And can you remind us when the application for the patent-in-suit was filed?

A. The application for the patent-in-suit was filed in July 2019.

Q. And can you remind us when the patent actually issued?

A. October 2020 on the far right of the picture.

Q. And, Doctor Lambert, if I can turn your attention to where it says, 'December 2015', what are you indicating on that slide?

A. In December of 2015, I'm indicating the date when Daiichi Sankyo actually presented Enhertu to the public.

Q. And what are you indicating on November 7th of 2017?

A. That Daiichi Sankyo was issued a patent covering various parts of the Enhertu structure.

Q. And then what are you indicating in 2018 and 2019?

A. Other aspects of Daiichi Sankyo's invention that covers Enhertu.

Q. And, Doctor Lambert, what are you indicating in green for March of 2019?

A. In green I'm indicating that Daiichi Sankyo and AstraZeneca entered into a collaboration to market and distribute Enhertu worldwide to cancer patients.

Q. And, Doctor Lambert, we see a bar at the top that says, "Seagen analyzes Enhertu". Is that of any significance to this question of non-infringement?

A. I believe it is.

Q. And can you explain to us why you believe it's of significance?

A. During -- once Daiichi Sankyo presented Enhertu to the public in December of 2015, I know it created a lot of interest in the ADC communities, at ImmunoGen as well, and it's clear that from the documents I've been able to look at that Seagen actually made the drug linker of Enhertu in their laboratories and actually to use it as a benchmark to test various other compounds against it. And certainly they spent two and a half years working with this compound before ever filing an application for this '039 Patent.

Q. And, Doctor Lambert, I'd like to show you DX 490.

THE COURT: Let me interrupt at this point before we go any further.

Ladies and gentlemen, it's now noon, and I'm told by the Clerk's Office your lunch is waiting for you in the jury room. This examination has some considerable length to go, and there's probably not a perfect place to break, but this is as good as any. And it's the noon hour, so we're going to break for lunch at this point.

If you would take your notebooks with you to the jury

room and, as I say, lunch should be waiting for you there. Please follow all the instructions I've given you, including, of course, not to discuss the case with each other. And we'll attempt to reconvene shortly before 1:00.

The jury's excused for lunch.

(Brief recess.)

THE COURT: The Court stands in recess.

(Lunch recess.)

THE COURT: Be seated, please.

Mr. Ratliff, are you prepared to continue with your direct examination?

MR. RATLIFF: I am, Your Honor.

THE COURT: All right. Doctor Lambert, if you'll return to the witness stand, please, sir. I remind you that you remain under oath.

And while he's -- go ahead. Have a seat at the witness stand.

THE WITNESS: Thank you, Your Honor.

THE COURT: Ms. Ainsworth, are you prepared to make the proffer that you mentioned earlier?

MS. AINSWORTH: I am, Your Honor. But if the Court would prefer, I can do it at the afternoon break.

THE COURT: All right. Just don't let us forget.

MS. AINSWORTH: Thank you, Your Honor.

THE COURT: All right. Let's bring in the jury,

please.

(Whereupon, the jury entered the courtroom.)

THE COURT: Welcome back from lunch, ladies and gentlemen. Please have a seat.

We'll continue with the Defendant's direct examination of Dr. John Lambert.

Mr. Ratliff, you may continue.

MR. RATLIFF: Thank you, Your Honor.

Q. (BY MR. RATLIFF) Doctor Lambert, let's bring up your slide 38.

A. Yes.

Q. And we were discussing this before, and I just want to turn your attention to the bottom of the slide that has the DX numbers 124 and 127.

Does this reference the Sankyo documents that you discuss on this slide?

A. Yes, they do.

Q. And let's turn to your slide 40.

And looking at the DX numbers in the bottom, we see DX 61, 62, 111, 112, 118, 123, 242, 243, and 693.

Are these references for what you've talked about in the timeline here?

A. They are.

Q. Thank you, Doctor.

So let's turn to your slide, Doctor. I'd like to talk to

you about the issue concerning validity in this case. Let's move to your slide 41.

And, Doctor Lambert, have you prepared slides that discuss your analysis on the issue of patent invalidity?

A. I have.

Q. And, Doctor Lambert, in your analysis, have you considered who is the POSA, the person of ordinary skill in the art?

A. Yes, I have.

Q. And can you explain to us who is that POSA?

A. The POSA would be -- or person of ordinary skill in the art would be someone that would have a Ph.D. in, say, biochemistry or chemistry or biology, or someone with a Master's degree and maybe five years of experience in the pharmaceutical industry.

Q. Now, Doctor Lambert, let's talk about the first bullet on your slide. Let's turn to slide 42.

And can you explain to us, Doctor, what you're indicating on this slide at a very high level?

A. What I'm indicating is that this patent only describes ADCs with monomethylvaline compounds, a Seagen's discovery.

Q. And, Doctor Lambert, have you undertaken a careful review of the patent?

A. Yes. I've reviewed all 200-plus pages of the patent.

Q. And do you have a slide that explains your analysis of

reviewing all of those pages of the patent?
A. I do.
Q. Let's turn to your slide 47.
And as we watch this, Doctor Lambert, can you explain to us what you're showing on your slide?
A. What I was showing is that everywhere in this patent the drugs that are attached to antibodies, that they only describe auristatin compounds, in particular MMAE and MMAF, which is consistent with the title and the abstract and the description of the drug moiety in the specification.
Q. Now, Doctor Lambert, let's turn our attention to DX 1, which is a copy of the patent, looking at column 31, beginning at line 39.
A. Yes.
Q. And, Doctor --
MR. RATLIFF: We're looking for column 31, starting at line 39.
Q. (BY MR. RATLIFF) Now, Doctor Lambert, you see there it says a chemotherapeutic agent?
A. Yes, I do.
Q. Did you read this portion of the patent?
A. I did.
Q. And can you explain to us what this portion of the patent talks about?
A. So this portion of the patent is talking about

chemotherapeutic agents that are useful in the treatment of cancer. It's essentially a long list of anticancer agents that are either used in the treatment of cancer at the time the patent was written, have been used, or were in clinical trials, hoped to be used. They are all cancer chemotherapeutic compounds.

Q. And, Doctor Lambert, is the discussion about chemotherapeutic agents in this patent a description of the drug moieties that the inventors discovered?

A. No, it is not.

Q. Do you have a slide that explains your analysis on this point?

A. I do have a slide on that.

Q. Let's bring up slide 50.

And, Doctor Lambert, at the top you say, chemotherapeutic agents are not drug moieties. Can you tell us why you have that belief?

A. Yes. So why I have that belief, that in the three places in the patent that talks about the chemotherapeutic agents, these agents that are designed -- that are listed to be included to treat cancer patients with the ADC together with the chemotherapeutic agents listed.

After all, much cancer treatment today is combinations of chemotherapeutic agents, and it was envisaged by the inventors that the ADCs of the invention could be used in combination

with existing cancer drugs.

Q. And, Doctor Lambert, can you explain to us what you're showing in that first box on the top of your slide?

A. So the first box is that the pharmaceutical composition comprise an effective amount of the antibody-drug conjugate together with a therapeutic amount of another chemotherapeutic agent.

Q. And can you explain to us what's described in the second box on your slide?

A. So the second box says that the exemplary conjugate of the invention, the ADC of the invention, can be administered to a patient concurrently with the chemotherapeutic agent. So at the same time.

Q. Can we turn to your next slide, Doctor?

Now, in your next slide, I see the words CHOP and FOLFOX. Can you explain what those refer to?

A. So CHOP, C-H-O-P, is actually an acronym describing a mixture of four different chemotherapeutic compounds. It's a chemotherapeutic regimen used to treat lymphoma patients today.

And FOLFOX is another acronym. Actually it's an acronym for a mixture of three different chemotherapeutic compounds that are used in chemotherapy today actually to treat colon cancers and some other cancers.

Q. And, Doctor Lambert, would the POSA be able to use CHOP

or FOLFOX as a drug moiety in the context of this patent?
A. No, it would be impossible.
Q. And can you explain why?
A. Because it's hard enough to design an ADC with one drug moiety as a -- as a payload. To contemplate attaching four different chemicals, four different agents, whose potencies vary across a wide range will be just impossible to actually achieve.
Q. Doctor Lambert, can we turn to your next slide?
And can you explain to us what is the significance of what you're trying to show on this slide to this case?
A. What I'm trying to show in -- in this case is that what is claimed in the '039 Patent, asking the question, is what is claimed described in the patent, in the 200-plus pages of the specification of the patent.
Q. And, Doctor Lambert, I see you have a column and rows and a table?
A. Yes.
Q. And can you explain to us how we are to understand your table?
A. Yeah. So what is described in the patent are monomethylvaline compounds of the auristatins of the invention, and they could be included in the claim. However, Enhertu's drug moiety, camptothecins, are not described as drug moieties even though they are included in the claim but

they are not found in the specification of the patent.

Similarly, what is claimed is any drug moiety, and that's not -- not described in the patent, that the invention, any invention, could be used for any drug moiety. In fact, what the specifications describe are monomethylvaline compounds.

Q. Doctor Lambert, can we turn to your analysis on the question of enablement?

A. Yes.

Q. Let's turn to your slide 53. And, Doctor Lambert, at a high level, what's your opinion with respect to the issue of enablement?

A. Well, at a high level, the patent specification just fails to teach how to make and how to use any of the innumerable number of ADCs that Seagen broadly seeks to claim.

Q. Now, Doctor Lambert, are all drug moieties able to be linked?

A. No, they are not.

Q. And do you have a slide to explain?

A. I do have a slide to show that.

Q. Let's turn to slide 55.

And, Doctor Lambert, in your slide 5 you write at the top, Seagen had to do significant research to make an attachable monomethylvaline drug moiety. Can you explain what you mean by that?

A. Yes. So the -- the toxication auristatin E had no

chemical handle to be able to attach it to an antibody. And Seagen's invention, in fact, described in this patent, in the specifications of the patent, was, in fact, to invent monomethylvaline compounds, for example, monomethylvaline auristatin E as the structure listed here, this is an auristatin that actually now has a chemical handle to enable it to be attached to an antibody. The chemical handle is colored by the yellow dot there.

Q. And, Doctor Lambert, on the right-hand side of this slide, you refer to new drug with chemical handle. Can you explain to us why that has any significance to this case?

A. What's significant, if you make any new chemical molecule, it actually is a new drug. It can behave differently in the body. It's been -- it is not the same as the drug that -- it is not the same as auristatin E, for example. So it's a new drug.

Q. Doctor Lambert, the exhibit numbers at the bottom of the slide, 71, 128, 129, 153, 208, what are they?

A. They are documents that support this contention here.

Q. Can we move to your next slide?

A. Yes.

Q. Now, Doctor Lambert, you write, Maytansine cannot be used as a drug moiety in an ADC. What are you referring to here?

A. Well, maytansine is actually a psychotoxic drug that ImmunoGen worked with, and the chemical structure is shown on

the right. Maytansine actually lacks a chemical handle to be able to attach it to antibodies with the technologies available at the time in the -- when we started working with it in the -- actually in the late 1980s, actually, and through the 1990s.

Q. And, Doctor Lambert, is maytansine referred to in the 2019 filed Seagen patent?

A. Yes. It's listed as an example of a chemotherapeutic agent that could be useful in the treatment of cancer. It was in clinical trials as a potential treatment for cancer. It was just too toxic to actually be useful as it turned out.

Q. And, Doctor Lambert, at the bottom there, there's DX 158.

Is this another exhibit that can be looked at for some information concerning what you discussed on this slide?

A. Yes, it is.

Q. Now, Doctor Lambert, do you have any experience with that maytansine drug moiety?

A. Yes. It's the drug moiety that ImmunoGen, the company I worked for, worked with.

Q. And do you have a slide to explain some of your experience?

A. And I do have a slide, yes.

Q. Let's turn to your next slide.

Now, Doctor Lambert, can you explain to us what you're intending to show here?

A. What I'm intending to show here is that ImmunoGen's research ultimately led to the development of a new drug, which we called DM1, which actually now has a chemical handle that enabled it to be attached to antibodies with certain linkers. And the chemical handle there is in the yellow box.

Q. And, Doctor Lambert, was this work easy to do?

A. No, it wasn't.

Q. How much time did it take?

A. Well, you can see from the slides, it took from -- having maytansine in our hands, it took about six years of chemistry to actually end up with making DM1.

Q. Now, Doctor Lambert, is it always possible to make a new ADC by linking a drug moiety?

A. Could you rephrase the question?

Q. Sure. I'll ask it this way. Is it always possible to make a new linkable drug from an unlinkable drug?

A. No, it is not always possible.

Q. And why not?

A. Well, in many -- the places where you could do chemistry to attach a chemical handle, the molecule you make, it might have a chemical handle but you may have destroyed the activity of the drug so it doesn't work. And so this is why it's a whole iterative process to try to figure out whether you can put a chemical handle on a given drug. And in -- and in quite a few cases, you just cannot.

Q. And, Doctor Lambert, the exhibit numbers here, DX 70, 79, 82, 85, 86, 161, 179, 190, 202, and 205, are they references that we could look at to learn more about the concepts you mentioned on this slide?

A. Yes, they are.

Q. Now, Doctor Lambert, are there other drugs that are unlinkable?

A. Yes, there are.

Q. And have you prepared a slide to show some examples?

A. I have. I've got --

Q. So let's turn to your next slide.

And, Doctor Lambert, can you explain to us what you're showing on this slide?

A. What I'm showing on this slide is a variety of drugs they're all listed in that really long list of chemotherapeutic drugs in the specification of the '039 Patent. And, actually, none of them have a chemical handle to allow them to be linked, and in many cases I don't see how you could even attach a chemical handle.

In any case, putting a chemical handle on would make a different drug entirely.

Q. And, Doctor Lambert, do you consider it to be routine chemistry to try to add this new chemical handle?

A. No, it isn't.

Q. And in the course of looking at informing your opinions

in this case, did you have an opportunity to hear Seagen's scientists talk about these concepts?

A. I did.

Q. And what was your understanding?

A. That it was actually difficult.

Q. Now, Doctor Lambert, I'd like to turn to another part of your analysis, so let's turn to -- may we turn to your slide 68 -- or 64?

A. Yes.

Q. And so, Doctor Lambert, your slide 64 says, "Many drug types were not attachable to make ADCs in 2004."

So, Doctor Lambert, can you explain to us what you're showing on the table in this slide?

A. So what I'm showing is a list of drug types on the left and whether they were attachable with the technologies available in 2004.

Q. And can you explain each of the rows, starting first with non-conjugatable?

A. So non-conjugatable drugs, those are those drugs where one just cannot find any place to put a chemical handle without destroying the activity of the drug.

Q. And can you explain what's referred to about tertiary amines?

A. A tertiary amine is a drug actually like auristatin that actually had no chemical handle to be able to attach it to a

drug. And, in fact, it's the basis of Seattle Genetics of monomethylvaline compounds. So it's actually converting a tertiary amine to a type of amine that could be used to attach.

Q. And, Doctor, how do the files relate to this analysis?

A. Files were not attachable to peptide-type drugs, peptide-type linkers in 2004.

Q. And, Doctor, can you explain to us how the second two or the last two remaining rows relate to your analysis on whether or not drug types were attachable in 2004?

A. Alcohols in general were not attachable. A special subset of alcohols, phenyls, were attachable by the technology available in 2004, but most alcohols were not. And anilines were not readily attachable, either, for a variety of reasons.

Q. Doctor, turning your attention to the bottom right-hand corner, we see DX 495.

Is that a reference that helps explain some of the concepts that you mentioned to us about the slide?

A. It is. It is.

Q. Now, Doctor Lambert, earlier you spoke to us about the functional requirement of the claims. What did you mean by that?

A. The claims of the '039 Patent not only describe a whole ADC, but also impose upon that whole ADC a particular functional requirement.

Q. And can we turn to your slide 65?
A. Yes.
Q. And, Doctor Lambert, at your slide 65, it reads, "The '039 Patent does not teach how to make and use the claimed ADCs without undue experimentation."
What are you showing on this slide, Doctor?
A. Yeah. So what I'm showing is the claim that is with highlights. So it claims an antibody-drug conjugate where D is a drug moiety, and that's any type of drug, not limited to an auristatin, and wherein the drug moiety is intracellularly cleaved in a patient from the antibody of the ADC.
Q. And, Doctor, is determining how an ADC functions complex?
A. It is complex.
Q. And do you have a slide explaining this complexity?
A. Yes, I do.
Q. Let's turn to your slide 67.
Now, Doctor Lambert, can you give us an overview of what you're trying to explain to us in this slide?
A. So what I'm trying to explain is that there are -- to determine how an ADC functions is that you have to understand whether an ADC linker can be cleaved; where the actual cleavage takes place in a patient, for example, is the ADC capable of reaching the cancer cells in the patient; and what products are released from the cleavage.
Q. Now, Doctor Lambert, does the '039 Patent teach this?

A. No, it does not.
Q. And is cleavage of ADCs something that occurs inside of the cells?
A. Not necessarily.
Q. Now, Doctor Lambert, can we -- we see there at the bottom of your slide, you referred to DX 75, 85, 93, 96, 140, 145, 191, and 219.

Are these also references about the concepts you are explaining to us today?
A. They are.
Q. Can we turn to your next slide?

Now, Doctor Lambert, what are you showing on the left-hand portion of this slide?
A. On the left portion of the slide, I'm showing three different ways that an ADC can be cleaved. They can release the drug moiety, the drug moiety with part or all of the spacer, or the drug moiety with the spacer and part of the peptide.

And these are just three of the -- of what -- of the things that could happen in the cell.
Q. And what are you showing on the right-hand portion of the slide?
A. So the right-hand portion of the slide is a -- is a picture image to match the statement. So if cleavage happens and all elements of the spacer fall off, you release the drug

moiety represented by the brown ball.

If cleavage happens and part of the spacer is still attached, you can see that by the little purple bar. It's now a different chemical and has part of the spacer attached.

And cleavage could happen within a peptide, for example, and so the released molecule is the drug -- the drug with part of the spacer and even amino acid, as represented by the green ball, still attached. And that could be the final payload within a cell, for example.

Q. Now, Doctor Lambert, you mentioned that some ADCs do not intracellularly cleave to release free drug, but can they still kill the cancer cell?

A. They can.

Q. And have you prepared a slide to explain how that might be possible?

A. I have.

Q. Let's turn to your next slide.

And can you explain to us what you're showing here on this slide?

A. So what I'm showing here on this slide is that many of the payloads released within cancer cells, they will kill cells.

So, for example, in the far right, the payload is just the drug moiety, the -- the ball. That will kill cells. It can also be released outside the cancer cells, but it will --

it will diffuse into cancer cells and kill them.

In the next one over, the -- the drug moiety still has part of the spacer. Attached in the bottom, it has part of the spacer and still the peptide attached because it happened to have a peptide that didn't cleave fully; or in the far left, it's the drug moiety with the spacer, and that blue symbol represents part of the antibody. So that would be a completely uncleavable link.

All of them, all of the molecules released within the cancer cell, could kill the cancer cell.

Q. Now, Doctor, at the bottom you referred to DX 136, 155, 169, 176, 181, 185, 216, and 220.

Are these references that we could look at to understand more about the concepts you just explained?

A. Yes, they are.

Q. Now, Doctor, let's take a look at DX 74. And this is a paper that we've seen before. And have you read this paper, Doctor?

A. Actually, this is a paper I authored amongst other authors from ImmunoGen.

Q. And can you tell us what you're talking about in this paper?

A. So in this paper we made a drug moiety and actually attached it to an antibody using a tripeptide. That's three units. And the three units were all glycine, or Gs. So it's

a GGG tripeptide.

Q. And what were the findings that you talk about in this paper, Doctor?

A. In brief, the findings were that in a -- if you look on the bottom left, in a lung cancer cell line called Calu, about a third of what was released in the cancer cell was the drug moiety, but two-thirds of it was the drug moiety still with a glycine from the linker attached. And --

Q. Excuse me, Doctor.

A. -- I was going to go on to say in the COLO 205 cells, which is a colon cancer cell line, and these are experiments conducted in a dish in cell lines, the released payloads either are the drug moiety with a glycine attached, or a completely uncleaved linker -- is actually the drug moiety with the glycine--gly gly gly--linker and a piece of the antibody. There is no free drug moiety within the colon cancer cell line.

Q. So, Doctor Lambert, on this issue of lack of enablement of Seagen's patent, what is the significance of your paper?

A. I think the significance of this paper is that even conducting experiments on cells in a dish, it is difficult to determine what the released drug moiety is in cancer cells, and it can even vary from cell to cell.

And this work was difficult. In fact, it comprised a whole scientific paper by itself. And to contemplate doing an

assay, have a routine assay that you could conduct on a patient's tumor, administered an ADC, is -- I think it just -- first, no such assay exists, and it would be really difficult to -- to figure out how to do that.

Q. Doctor, was it routine for you to attempt to determine whether your ADCs intracellularly cleave when you did such research in the 2010s?

A. No, it was not. As evidenced by -- actually this was a substantial amount of work that comprised the scientific paper by itself.

Q. Now, Doctor Lambert, can we take a look at DX 75? Do you recognize this paper?

A. I do.

Q. And it says at the top, an industry white paper. Do you see that?

A. Yes, I do.

Q. And can you explain to us what's meant by an industry white paper?

A. It's a paper produced by a collaboration amongst many in the -- many representatives of different companies to -- to actually harmonize approaches to study the absorption distributions on the properties of a drug in people.

Q. And, Doctor Lambert, if we could turn your attention on the slide, I believe there's a call-out from page 5 --

A. Yes.

Q. -- of 7. Can you explain to us what's the significance of what's shown in this call-out?
A. So I think what's significant here is that -- the point the authors are making, to select a cell line to determine the activity of an ADC as a routine assay would be very difficult and can't be standardized and used across multiple programs.
Q. Now, Doctor Lambert, can we turn to your opinions regarding whether Seagen's 2019 filed patent lacks priority?
A. Yes.
Q. Let's turn to your slide 70.
And, Doctor, can you give us a brief overview of your opinion on that issue?
A. So my opinion here is that the patent lacks priority because ADCs with a G- and F-only tetrapeptide, the first time they are mentioned at all is in the July 2019 application. It is not in the 2004 application nor in any of the 200 pages of specification that come before the claim.
Q. And since you're talking about time, Doctor, do you have a timeline that helps us understand better your analysis?
A. I do.
Q. And can we turn to your timeline?
A. Yes, certainly.
Q. Let's turn to DX 73. And, Doctor Lambert, what are you showing here on this slide?
A. There I'm showing the date that Seagen filed the 2004

patent.
Q. And what did you see in this particular 2004 application?
A. I saw that it actually had, with regard to the peptide linker, basically a description that was essentially a kitchen sink of many, many, many possibilities.
Q. And can we turn to the next point on your timeline?
And, Doctor Lambert, what are you showing here?
A. I'm showing in December 2015, the date that Daiichi Sankyo presented Enhertu to the public at a -- at a scientific meeting that I attended, actually.
Q. And let's take a closer look, Doctor. Let's turn to your next slide.
A. Yes.
Q. And I believe this is the paper that we've seen before, but can you give some more context to how this paper fits in your analysis with respect to the question of lack of priority?
A. Yes, because this presentation, this is the poster that was presented at the meeting, it was the first time any ADC that I had seen or anyone else that had a G/F-only tetrapeptide as within the linker that connected the drug moiety to the antibody.
Q. And, Doctor Lambert, can we turn to your next data point on the timeline?
A. Yes.

Q. And I see it looks to be an October 2019 time point. Can you explain to us what you're indicating there?
A. Yes. In October 2019 was when Seagen filed patent claims to an ADC with a G/F-only tetrapeptide.
Q. And what are you highlighting there in the middle, Doctor?
A. What I'm highlighting in the middle is the part of the claim where each Ww unit is a tetrapeptide and going on with a further description that is describing a tetrapeptide, that is, four building block amino acid unit, where the amino acids can only be one of two types--G or F.
Q. And, Doctor Lambert, can we turn to your next point with this slide?
A. Yes. So this point is that from the disclosure in the 2004 patent, which is just a kitchen sink of millions of possibilities, to actually the specific narrow claim of a tetrapeptide containing only G or F, there is no way of getting from the left to the right without the knowledge of the publication, if you like, of the DS-8201, the ADC of Enhertu with a G/F-only tetrapeptide.
Q. Now, Doctor, do you understand that Seagen says its 2019 filed patent is entitled to a 2004 priority date?
A. I do.
Q. And you've analyzed that question. Right?
A. I have analyzed the question.

Q. And if we turn to your next slide, and let's turn one slide further.

On that particular question, what was your conclusion?

A. My conclusion was that Seagen didn't -- nor anyone else, for that matter, thought of a G/F-only tetrapeptide and the first time it was seen was with the Daiichi Sankyo publication in 2015.

Q. And so in your opinion, Doctor, does that -- what does it mean with respect to the issue of does Seagen's 2019 patent application have priority back to 2004?

A. I would say that it does not have priority back to 2004 because no ADC was made with a G/F-only tetrapeptide, and there is no -- just no finding of that in all the 200 pages of the -- of that 2004 filing.

Q. Doctor, can we turn to --

MR. CHIVVIS: Your Honor, we object to that question and move it be stricken as legally irrelevant to whether priority is met do not need to have a physical embodiment of your patent in order to disclose the elements of the invention. And the witness' testimony suggested that they needed to have made the embodiment in order for the patent to properly claim priority. We think that's improper.

THE COURT: You can certainly address that on cross-examination. Objections to improper questions need to be raised before the witness completes their answer and it's

in the record. Again, your objection's untimely.

And I understand you may have some difficulty getting up and down out of your chair. You can make your objection sitting if you want to. But unless I hear them before the answer is completely in the record, I'm going to consider them untimely.

Let's proceed.

Q. (BY MR. RATLIFF) Doctor, can we turn to your next slide?

A. Yes, certainly.

Q. Now, actually before we get there, let me ask you some questions.

Doctor Lambert, so let's turn to the 2004 application, and let's bring up DX 7.

A. Yes.

Q. And do you recognize this, Doctor?

A. This is the cover page of the original filing in November 2004.

Q. And did you review the 2004 application and its file history when you did your analysis with respect to priority and anticipation?

A. I did.

Q. And based upon your review, did you ever see anything within those documents that referenced an ADC with a G/F-only tetrapeptide?

A. No. There is no mention at all of an ADC with a G/F-only

tetrapeptide.
Q. And, Doctor, did you also review -- in addition to the patents, did you review the provisional applications and file histories of the other patents in the family?
A. I did.
Q. And those documents, DX 2 was one of the patents we looked at before. Right?
A. Yes, it was.
Q. And do you recall that you also looked at DX 3 through DX 16?
A. Yes.
Q. Now -- and based upon your review of all of that information, Doctor, did you see any reference to an ADC with a G/F-only tetrapeptide?
A. No. There were no references at all.
Q. Now, Doctor, can you -- can you describe for us what is disclosed in the 2004 application concerning amino acids?
A. What is disclosed is a very large number of amino acids that could be possibilities to apply to a peptide linker.
Q. And do you have a slide that explains what those amino acid possibilities are?
A. I do have a slide that so explains.
Q. And what are you depicting here on this slide?
A. So on the left of the slide, I'm depicting the page in the patent specifications, and in the bluey gray is a listing

of all the possible structures of amino acids. And when you go through all of those structures and analyze them, you end up with 83 different options for each position of a peptide.

Q. And, Doctor Lambert, do you have a slide that helps us understand better to picture in our heads these 83 different amino acids?

A. Yes, I have because, you know, these listings are just names and words and chemical structures. I actually have an image here of different building blocks, 83 different building blocks that represent the different shapes and activities and structures of 83 different antibodies.

Q. And do you have a slide that explains what are --

A. Sorry. 83 different amino acids.

Q. Thank you, Doctor.

Doctor, do you have a slide that explains what the 2004 application discloses using these 83 different amino acids?

A. I do have a slide that shows that.

Q. Let's turn to your next slide.

And, Doctor Lambert, what are you showing here in the graphic on this slide?

A. What I'm showing in the graphic is that the peptide of which -- so each position has 83 possibilities. The peptide can vary from actually having no peptide at all, zero, or having one amino acid unit or 2 amino acid units all the way up to 12. So there are 13 different options in length from 0

to 12.

Q. And, Doctor Lambert, do you have a slide that helps us understand the information that's described in the patent about how to connect the 83 amino acids to make peptides?

A. I do have a slide that describes what information is in the specifications, yes.

Q. Can we turn to the next slide?

So, Doctor, we just saw an animation. Can you explain to us what you were intending to convey with this slide?

A. What I'm intending to convey is the number of -- is an example of a dipeptide, tripeptide, all the way up to a 12-unit peptide. I didn't need to show none or one. And just an example of a dipeptide, for example, the dipeptide has a green A and a pink R. That's just a dipeptide. But it's just an idea to represent the shapes and structures of different amino acids in peptides.

Q. And let's turn to your next slide.

What are you showing here, Doctor?

A. What I am trying to illustrate here, if you just take a four-unit peptide and at each position of the four units, first, position one, there are 83 options; then at position 2, there are 83 options, so that's 83 times 83. And then at position 3, there are 83 options. If you add that up, in tetrapeptides alone there are 47 million options.

Q. And, Doctor Lambert, are any of these examples G/F-only

tetrapeptides in the patent?
A. There are three tetrapeptides specifically mentioned in the patent, and none of them are G/F-only.
Q. And now, Doctor, we heard from Doctor Bertozzi talk about dipeptides with G and F that were made by Doctor Kline in 2004.
In your opinion, Doctor, do they provide any support in this patent for G/F-only tetrapeptide ADCs?
A. No, they don't. They are dipeptides, not tetrapeptides.
Q. And, Doctor Lambert, do you have a demonstrative that illustrates the exemplary peptides from the 2004 application?
A. I do.
Q. Can we turn to your next slide?
And what are you showing here, Doctor?
A. What I'm showing here are the specific dipeptides, tripeptides, or tetrapeptides that are actually described within the specifications of the '039 Patent.
Q. And can you explain to us the different shapes and colors?
A. So, for example, the amino acid F, or phenylalanine that you've heard of, I use as a black triangle. Glycine that you've also heard of, if you look in the bottom right, it's one of the amino acids in a tetrapeptide, is a purple square.
So I've tried to use the same symbol for the same amino acid and this represents the peptides that are used or at

least described within the specification of the patent.

Q. And at the bottom of your slide, Doctor, it refers to DX 142, 177, 213, 214, 215, 218, and 244.

Is this information supporting what you're describing to us on this slide?

A. It does, yes.

Q. Now, does the 2004 application contain any data or indication that any of the examples were ever made and actually tested?

A. Yes, it does.

Q. And do you have a demonstrative explaining and showing what were those examples?

A. Yes, I have.

Q. Let's turn to your next slide.

And what are you showing here, Doctor?

A. What I'm showing here is that the only ADCs actually made and tested within the patent specifications use one of only two of the particular dipeptides that were -- were described where you've got a V and Cit, actually that's the commonly known val Cit; or F and K, that's phe and lysine; the val Cit dipeptide is the one that Seagen is well known for for use in attaching its monomethylvaline compounds within ADCs.

Q. And, Doctor, do you have a slide explaining how these examples compare to the large mountain that we saw of amino acids?

A. I do.
Q. Can we turn to your next slide?
Can you explain to us what you're showing here, Doctor?
A. What I'm showing here is that the ADCs actually made and tested and described therefore in the '039 Patent which just have two dipeptides, cannot possibly lead to G/F-only tetrapeptides, and you couldn't find it from that large mountain of 47 million possibilities.
Q. Now, Doctor, let's return back to your timeline, and let's move ahead. We have this next event. And what is the date we see here in December 2015 again?
A. That's the date that Daiichi Sankyo scientists presented Enhertu at a public meeting.
Q. And then what do you have on the right underneath that structure that we saw before?
A. On the right I have the structure of the G/F-only tetrapeptide using the same symbols that I had described in -- or used in those earlier pictures as representations of the structures.
Q. And, Doctor Lambert, can you remind us again, what is that structure behind -- right above your depiction of GGFG-only tetrapeptide?
A. Yes. The structure right above GGFG is the structure of Enhertu.
Q. And can we turn to the next event on your timeline, which

is slide -- let's go to slide 91.

And with respect to slide 91, what are you showing here, Doctor?

A. What I'm showing here is the first time Seagen filed patent claims to an ADC with a G/F-only tetrapeptide, and it's the first time that the G/F-only tetrapeptides were mentioned at all in the file history.

Q. And, Doctor, do you have something to visually help us understand what were the group of G/F-only tetrapeptides in an ADC that Seagen sought to claim?

A. I do.

Q. Can we turn to your next slide?

And what are you showing here, Doctor?

A. Well, if you construct a tetrapeptide of only G and F, there are only 81 possibilities. I just draw 16 of them here for illustration.

And the other thing I show is that the F -- you notice the F triangle could be right-side up or upside down. That's because the amino acid phenylalanine has two flavors, actually, from the structure, if you think one is right-handed, one is left-handed. The amino acid glycine only has one form.

Q. And, Doctor, is -- how did you arrive at the 81 G/F-only tetrapeptides?

A. So if position 1 just has three possibilities, either

glycine or F in one of its two forms, so it's three possibilities; if the second position has three possibilities, that's three times three; if the third position has three possibilities, that's times three again; and if the fourth position has four -- that's times three again, you end up with 81.

Q. And, Doctor Lambert, I see here you have a reference here at the bottom of the slide 217. Is that something that can be referred to to understand the concepts on this slide?

A. Yes, it is.

Q. And, Doctor Lambert, do you have a summary slide that starts to show your analysis on the issue of priority?

A. Yes, I do.

Q. Can we turn to the next slide?

And so what is the ultimate conclusion that you have, Doctor, with respect to this issue of priority?

A. On the issue of priority, so Seagen -- the first time the -- that G/F-only tetrapeptides are mentioned is in 2019. You could not find them in the specification filed in 2004. It would be impossible to actually predict the G/F-only tetrapeptide would be what you were looking for. And so the earliest priority should be October 2019.

And, again, another fact in that is that by 2015, G/F-only tetrapeptides were now in the public domain. Scientists knew about them. It was out there.

Q. And, Doctor Lambert, you said -- I think you said that the earliest priority should be in October of 2019?
A. That's the first time G/F-only tetrapeptides were ever mentioned in any of the file history of this patent.
Q. Now, Doctor Lambert, do you have a slide that shows how the claimed ADCs with G/F-only tetrapeptides compared to the entire disclosure of the 2004 application?
A. I do.
Q. Can we turn to your next slide?
And what are you showing us here, Doctor?
A. This is just an illustration to show that the 2004 application, if you were to pick tetrapeptides from the -- going from 0 to 12--that's already an 'if'--if you were to pick tetrapeptides, there's 47 million possibilities.
There's no -- there's no way that you could go from there to find that a G/F-only tetrapeptide were what would actually make an ADC work.
Q. And, Doctor Lambert, do you have a slide that actually visually shows how the claimed ADCs with G/F-only tetrapeptides compares with the actual examples in the 2004 application?
A. Yes, I do.
Q. Can we take a look at that?
A. Yes.
Q. And, Doctor Lambert, can you explain to us what you're

showing on this slide?
A. So what I'm showing on this slide is in the left, the only ADCs made and used as examples within the specifications of the '039 Patent, the only ones made used one of only two different dipeptides.
And as you can see the structures, I don't think there's any way you would be able to -- any scientist or POSA would be able to say, Okay, these two dipeptides work; okay, now a G/F-only tetrapeptide will work. Actually that's an impossible leap to make.
Q. And does the 2004 application anywhere describe the specific group of 81 G/F-only tetrapeptides that are part of the claims?
A. Could you repeat the question?
Q. Sure. Does the 2004 application anywhere describe the specific group of 81 G/F-only tetrapeptides that are part of the claim?
A. No, not at all.
Q. And, Doctor Lambert, you're an avid hiker. Right?
A. I am. I hike in White Mountains National Forest in New Hampshire regularly.
Q. And are you familiar with the concept of blazemarks?
A. I'm very familiar with blazemarks. I would get lost in the forest without them.
Q. And can you explain to the jury what you mean by this

concept of blazemarks?
A. So a blazemark is a mark on a tree, typically a slash of paint, that enables you to keep on the trail and not get lost in the forest.
Q. And can you explain to us, does the concept of blazemarks -- also can be applied to a patent?
A. Yes, it can.
Q. And in this situation, are there any blazemarks to direct the person of ordinary skill to the claimed ADCs with G/F-only tetrapeptides?
A. In my opinion, there are none whatsoever.
Q. And can we turn to your next slide, Doctor?
And do you recall that Doctor Bertozzi had this slide; not your title, but she showed this slide during her presentation?
A. I do recall that.
Q. And at the top in your title you say, "No blazemarks to ADCs with G/F-only tetrapeptides in the 2004 application."
So, Doctor, what is your opinion of Doctor Bertozzi's analysis on this issue?
A. I disagree with her opinion.
Q. And have you prepared a demonstrative to illustrate your conclusion and disagreement with Doctor Bertozzi's opinion?
A. I have.
Q. So let's play that animation.

And so what did we just see, Doctor?

A. What I was attempting to illustrate here is that when Doctor Bertozzi highlighted tetrapeptide and glycine and phenylalanine, she was actually providing blazemarks to the tetrapeptide, except she was adding them on the slide. They do not exist in the patent.

The patent, as you see, the page in the patent is on the left and the representation is that there's a mountain of tetrapeptides, 47 million, that could be possibilities, and there are no blazemarks to lead you to say that a G/F-only tetrapeptide was the right one or even useful.

Q. And, Doctor, do you recall that Doctor Bertozzi suggested that the POSA would look at one of the 17 examples in the 2004 application and change it to create ADCs with new tetrapeptides?

A. I do remember her saying that.

Q. And can we turn to your slide 98?

And what are you explaining here on this slide?

A. What I'm explaining here is that the only two peptides used, which are dipeptides with just two amino acids, these are the only two peptides used in ADCs that worked, and so they're not tetrapeptides at all.

Q. And can we bring up PX 21?

And, Doctor, can we turn to page 8 of this?

And do you recall that Doctor Bertozzi testified about

these experiments?
A. I do.
Q. And were any of these experiments in Seagen's patent?
A. No, they were not.
Q. And from your recollection, did the person that conducted these experiments, Doctor Kline, test any G/F-only tetrapeptides in these experiments?
A. No, she didn't. These are all difficult peptides.
Q. So, Doctor, what is the relevance, if any, of these experiments of Doctor Kline to the issue that we're discussing with respect to lack of priority?
A. I would say none because, one, they're not in the patent; and, two, they're dipeptides anyway.
Q. Now, can we also turn to PDX 3.29?
And, Doctor, did you hear Doctor Bertozzi testify about this page from Doctor Kline's laboratory notebook?
A. I did.
Q. And what, if any, significance does what's shown here have on the question of priority?
A. In my view, none.
Q. And can you explain why?
A. Because it's -- first, it's not a G/F-only tetrapeptide, and it's not in the patent in any case.
Q. Now, Doctor, would any articles from before the 2004 application have provided clues how to make ADCs with G/F-only

tetrapeptides?
A. Could you repeat that question again?
Q. Sure. Would any articles before the 2004 application have provided clues to make ADCs with G/F-only tetrapeptides?
A. I would say no.
Q. And did you review the articles that Doctor Bertozzi referred to in her analysis?
A. Yes, I did.
Q. And what do you think about those articles?
A. The articles didn't provide any information to suggest that tetrapeptides would be useful in ADCs.
Q. And can we take a look at DX 538?
MR. RATLIFF: And let's blow it up.
Q. (BY MR. RATLIFF) And do you recognize this, Doctor Lambert?
A. I do.
Q. And what is it?
A. It's a list prepared by Doctor Kline, who was with Seattle Genetics, prepared in December of 2004.
Q. And are any of the tetrapeptides found in this list G/F-only tetrapeptides?
A. No, none of them are.
Q. And so what's the significance of anything of what's found here with respect to the question of priority?
A. I think this list has -- is -- has no relevance to the

issue of priority.

Q. Okay. Now, Doctor, can we turn to your slide 100? And I think we've seen this before.

Can you explain whether what's shown here is consistent or inconsistent with your opinion that Seagen did not describe the claimed invention in 2004?

A. This is consistent with my opinion. The Seagen scientists were very impressed with this drug linker as well.

Q. And why -- what about what you are showing on this slide indicates to you that it's consistent with your analysis on the issue of priority?

A. Because it is clearly stated that the Seagen scientists say that the drug linker is from Daiichi Sankyo, and later on in the document that they talk about the linker in DS-8201, which is Enhertu, was made using Daiichi Sankyo's proprietary payload and linker payload technology.

Q. Now, can we turn to your next slide, Doctor?

And on your next slide, Doctor, you have a slide called, "Seagen called it Daiichi Sankyo's linker before this lawsuit."

Can you explain to us what you're trying to explain to us by this slide?

A. Yes. What I'm trying to convey is that following the publication of Daiichi Sankyo's structure for Enhertu in December 2015 through 2016, and in this case 2017, in an email

from Doctor Jeffrey to Doctor Senter, they are making in their labs ADCs using the camptothecin drug linkers of other companies, and they refer to Daiichi Sankyo's drug linkers and they have a picture of GGFG, Daiichi Sankyo's drug linker.

Q. So, Doctor, is this information consistent or inconsistent with your opinion that Seagen's patent is invalid?

A. It's consistent with my opinion that it's invalid.

Q. And, Doctor, in the bottom right-hand corner, you referred to the DX Exhibits 461 and 571. Are those references to the documents that you're referring to on your slide?

A. They are.

Q. So if we can turn -- can we turn to your slide 102?

And so, Doctor, it looks like we see a timeline again.

A. Yes.

Q. Can you walk us through what is your conclusion as to whether or not the '039 Patent is entitled to priority all the way back to 2004?

A. My opinion is that it is not entitled to a priority all the way back to 2004 because the specification of the patent does not describe a G/F-only tetrapeptide and does not describe any blazemarks of how one would actually get to a G/F-only tetrapeptide from just the kitchen sink of disclosure of possibilities.

Q. And, Doctor Lambert, have you formed a conclusion as to

whether or not the '039 Patent is invalid for anticipation?
A. Yes, I have.
Q. And have you prepared a demonstrative to help illustrate that conclusion?
A. Yes, I have.
Q. So let's turn to your next slide -- or let's go back.
And so what is your conclusion, Doctor?
A. Actually my conclusion is that Seagen was not in possession of any information suggesting a G/F-only tetrapeptide was good for -- as a linker in an ADC until they saw it in the December 2015 disclosure from Daiichi Sankyo.
Q. And if we turn to your slide 105. Can we turn to that, Doctor?
And, Doctor, if we just assume for the moment that Seagen's assertion that Enhertu infringes is somehow correct, would the reference that we're looking at here on this slide anticipate Seagen's claims?
A. It would, because this publication describes the G/F-only tetrapeptide and the structure of Enhertu in March of 2016, well before the patent-in-suit was filed in 2019.
Q. Can we turn to your next slide, Doctor?
A. Yes.
Q. And did you also hear testimony from Doctor Senter discussing the -- did you also review testimony from Doctor Senter stating in his opinion that the reference Ogitani 2006

taught each and every limitation of the claims?

A. Yes, I did.

Q. And so -- can we turn to your next slide, Doctor?

And so what conclusions have you reached in this case, Doctor?

A. So the conclusions I reach is that Enhertu, in my opinion, does not meet all the claim limitations, so the patent is not infringed. If you were to suppose that it did meet the claim limitations, the patent is invalid because the information was already publicly available before the patent was filed.

Q. Thank you, Doctor.

MR. RATLIFF: I pass the witness.

THE COURT: Ladies and gentlemen, before we move to cross-examination of Doctor Lambert, we're going to take a short recess. You can simply close your notebooks and leave them in your chairs, follow all my instructions about your conduct, and we'll be back shortly to continue with this witness. We'll try to keep this short.

The jury's excused for recess.

(Whereupon, the jury left the courtroom.)

THE COURT: The Court stands in recess.

(Brief recess.)

THE COURT: Be seated, please.

Ms. Ainsworth, are you prepared to make your proffer?

MS. AINSWORTH: I am, Your Honor?

THE COURT: Third time's charm. Go ahead.

MS. AINSWORTH: Mr. Chivvis has agreed to share the microphone with me for a moment.

Your Honor, based on the Court's rulings in chambers this morning and decisions with regard to certain offered deposition testimony, Defendants wish to make a proffer of testimony and offers that the Court, we understood, overruled this morning.

Those are from Scott Jeffrey, lines 103 -- page 103, lines 8 to 13; page 169, lines 2 to 6; page 168, lines 24 to 25; page 181, lines 11 to 22. From Robert Lyon, page 213, line 22 to 214, line 2. And from Toni Beth Kline, page 17, line 6 to 7; page 17, lines 9 to 12; page 285, line 19 to 286, line 13.

And I have marked a copy of the transcript that I can tender to the Court.

But, in addition, Your Honor, Defendants would maintain their objections to Seagen's counterdesignation of Doctor Kline's testimony, which we understood that the Court overruled Defendant's objection this morning.

And this testimony was precluded by Defendant's motion in limine because they reflect Seagen's internal testing that was not included in the patent or priority applications and, therefore, is irrelevant and prejudicial under Rule 402 and

403.

Those page and lines are page 372, line 16 through 373, line 15; 373, lines 17 to 21; page 377, lines 17 to 24; page 378, lines 5 through 8; and page 378, lines 10 through 13.

Last, Your Honor, Defendants maintain their objections to Seagen's counterdesignation of Doctor Doronina's testimony at the following pages and lines: It would be 101, lines 3 to 5; 101, line 7 to 12; page 136, line 6 to 7; and page 136, lines 9 to 13, which we understood that the Court had overruled this morning.

THE COURT: Thank you, Ms. Ainsworth.

MS. AINSWORTH: And may I approach with the marked page and lines --

THE COURT: You may deliver it to the Courtroom Deputy.

MR. HILL: Your Honor, may Plaintiffs make a notation in the record with regard to that offer just for purposes of completeness?

THE COURT: Yes, you may, Mr. Hill.

MR. HILL: Thank you, Your Honor.

Your Honor, for purposes of completeness, Plaintiff would state with regard to the testimony of Doctor Jeffrey, Doctor Kline, Robert Lyon, and the additional portion from Doctor Kline that the Court allowed, and then the portions that the Court excluded that Defendants had wished to offer, the Court

excluded those in accordance with Plaintiff's Motion in Limine No. 9, and also on the basis of 402 and 403 concerns, which we believe the Court rightly decided.

But we wanted to flag for the record the basis for those exclusions.

THE COURT: All right. I'll consider the proffer has been made.

Are you prepared to go forward with cross-examination, Mr. Chivvis?

MR. CHIVVIS: Yes, Your Honor.

THE COURT: All right. Let's bring in the jury, please.

(Whereupon, the jury entered the courtroom.)

THE COURT: Please be seated, ladies and gentlemen.

We'll continue with the examination of Dr. John Lambert, and Plaintiffs will cross-examine the witness at this time.

Mr. Chivvis, you may proceed.

MR. CHIVVIS: Thank you, Your Honor.

THE COURT: Are there binders to distribute?

MR. HILL: Yes, Your Honor.

THE COURT: Let's do that first.

(Pause in proceedings.)

THE COURT: Let's proceed with cross-examination.

CROSS-EXAMINATION

BY MR. CHIVVIS:

Q. Good afternoon, Doctor Lambert.
A. Good afternoon, counsel.
Q. Doctor Lambert, we've met before, albeit remotely over a video platform. Right?
A. Yes, we have.
Q. I took your deposition some time ago.
A. Yes.
Q. Now, I'd like to just go over your background a little bit.
You're here today to testify on behalf Defendants. Correct?
A. I am.
Q. And I think you told us earlier you used to work at an ADC company called ImmunoGen. Right?
A. I did.
Q. Before that, you worked at Dana-Farber Cancer Institute in Boston. Right?
A. I did.
Q. And at Dana-Farber, I don't think you mentioned this in your testimony, you actually worked fairly closely with Dr. Peter Senter at Seagen. Is that right?
A. I did. He didn't mention it in his testimony, either.
Q. So you both know each other.
A. We do.
Q. And back at the Dana-Farber in the '80s, you were both

working on amino conjugates. That's kind of a predecessor technology to ADCs. Is that right?

A. That's correct.

Q. In fact, you and Doctor Senter at one time used to have house visits together. Isn't that true?

A. We did.

Q. Go out for beers together. Isn't that right?

A. Sometimes.

Q. How long has it been since you've been out for a beer with Doctor Senter?

A. It would be some time ago now. I mean, I see him at ADC meetings, but generally we don't socialize very much at those.

Q. Now, Doctor Lambert, you'd agree with me that Doctor Senter, because he was with you back in those days at Dana-Farber, also has about 40 years of experience in ADC technology. Right?

A. Yes, I would agree.

Q. And Doctor Senter left to go to Bristol Myers and then Seagen. Right?

A. Yes.

Q. And you left Dana-Farber to go to ImmunoGen in 1987.

A. Yes.

Q. I'd like to pull up your demonstrative slide No. 7 from your presentation today, Doctor Lambert.

A. Uh-huh.

Q. This is a slide you showed to the jury earlier today. Isn't that right?
A. It is.
Q. And you're here listing early innovators in the ADC field. Right?
A. Some of them.
Q. Some of them. Right?
A. There are a few not mentioned I know.
Q. Yeah. I'm going to get to that in a moment. Let's start with the ones you have on your slide.
Now, we just talked about ImmunoGen. That was the company that you joined upon leaving Dana-Farber.
A. Yes.
Q. And you mentioned in your presentation today--I hope I pronounce this right--NeoRx?
A. Yes.
Q. It's not NeoRx. It's NeoRx?
A. At the time the company existed, I think people called it NeoRx.
Q. NeoRx. And you have this other one, Cetus?
A. Yes.
Q. And you've got Sanofi?
A. Yes.
Q. Xoma?
A. Yes.

Q. Celltech?
A. Yes.
Q. Wyeth?
A. Yes.
Q. Immunomedics?
A. Yes.
Q. Lilly and CytoGen?
A. Yes.
Q. I want to focus on a few of these. I think you've already testified to this, but ImmunoGen has been involved in the creation of one approved ADC. Is that right?
A. Yes.
Q. Just one.
A. So far.
Q. Right. To date, the company ImmunoGen has only gotten one FDA approval for an antibody-drug conjugate. Isn't that right?
A. Correct. There's another one under review as we speak.
MR. CHIVVIS: I'd like to ask the Court to help confine the Doctor to his answers, but --
THE COURT: If your objection is that the witness is non-responsive, I'll sustain it, at least after he answered the question and then said, there's another one under review. The additional statement of, and there's another one under review, was not called for by the question, and it's

non-responsive, and I'll strike that from the answer.

And I'll remind the witness that he's here to give full answers but not to go beyond the scope of the question asked.

THE WITNESS: Yes, Your Honor.

THE COURT: And we'll proceed on that basis.

MR. CHIVVIS: Thank you, Your Honor.

Q. (BY MR. CHIVVIS) Let's talk about NeoRx, one of the other companies you mentioned in your presentation today.

A. Uh-huh. Yes.

Q. NeoRx doesn't have any approved ADCs. Is that right?

A. Nope.

Q. Excuse me. Just so the answer is clear, no, that's not right or --

A. No, it does not have any approved ADCs. I don't think it exists as a company.

Q. And let's talk about CytoGen. That's another one of these that you focused on in another one of your slides. Does CytoGen have any approved ADCs?

A. No, it doesn't.

Q. Does Cetus have any approved ADCs?

A. No, it doesn't.

Q. Does Sanofi have any approved ADCs?

A. Not yet.

Q. Does Xoma have any approved ADCs?

A. No, it doesn't.

Q. Does Celltech have any approved ADCs?
A. Their successor company of Celltech-Wyeth, which is now Pfizer, does have approved ADCs with the technology developed with Celltech and Wyeth in collaboration.
Q. Okay. So Celltech has a couple, and those use the acid cleavable linker technology that Doctor Bertozzi talked about in her testimony on Tuesday. Right?
A. That's correct.
Q. Different than the peptide linkers that Seagen has developed.
A. That's correct.
Q. They're not protease cleavable and they're not cysteine conjugated. Right?
A. That's correct, though you did make an error in your statement.
MR. CHIVVIS: Objection, non-responsive.
THE WITNESS: Excuse me, yes.
THE COURT: Sustained.
Q. (BY MR. CHIVVIS) So the acid cleavable ADCs that we talked about, that will cover Celltech and Wyeth.
Now, Doctor, Lilly doesn't have any approved ADCs, does it.
A. Not yet.
Q. You mentioned earlier that this slide may not be complete. You recall that?

A. Correct.
Q. And there's a big name missing from this slide, isn't there?
A. There's probably more than one name, but there is one big name missing and that's Bristol Myers Squibb.
Q. And another big name that's missing is Seagen. Right?
A. No. This -- it is missing, but this slide was specifically about companies existing in the 1980s.
Q. I don't see 1980s on this slide.
A. I said it in words.
Q. Okay. So you're talking only about the 1980s. Did all of these companies exist in the 1980s?
A. They were all active in the ADC field early in the 1980s, yes.
Q. But not too many have been successful. Isn't that true?
A. That's true.
Q. Seagen --
A. It's a difficult field.
Q. Seagen has been very successful in the ADC field, hasn't it?
A. It has.
Q. And you'd agree with me that Seagen is a company that is viewed as one of the leaders in the field of antibody-drug conjugates. Isn't that right?
A. Certainly.

Q. Bristol Myers exclusively licensed and spun off its entire ADC program into Seagen, didn't it?
A. It did.
Q. So when you say BMS is missing from this slide, you are talking about technology that Seagen inherited.
A. Yes.
Q. Now, I'd like to talk a little bit more about ImmunoGen.
A. Okay.
Q. In the late '90s, early 2000s, ImmunoGen was still a small company. Right?
A. Yes.
Q. And it relied on collaborations, didn't it?
A. It did.
Q. And sometimes it relied on collaborations with much bigger companies than itself --
A. Yes.
Q. -- including big pharma companies. Right?
A. Several.
Q. And also much bigger biotech companies. Isn't that true?
A. Not always true. One was a smaller company than ours that we had a collaboration with.
Q. Okay. But ImmunoGen had a collaboration with GenenTech. Right?
A. It did.
Q. GenenTech at the time was a much bigger company than

ImmunoGen. Right?
A. Yes.
Q. And that collaboration eventually led to an ADC, as you testified.
A. It did.
Q. Now, when ImmunoGen came to that collaboration, you were fairly high up in the organization at the time. Right?
A. Yes.
Q. And were you involved in the collaboration?
A. Yes.
Q. As part of that collaboration, there would have been know-how exchanged. True?
A. Correct.
Q. And there would have been an expressed agreement on guidelines about that know-how only being used for the collaboration and not for anything else by the other party to the deal. Isn't that right?
A. It was an understanding.
Q. It was an understanding that was probably reduced to writing. True?
A. All contracts have confidentiality clauses in them.
Q. And there was a confidentiality clause in the overall agreement between ImmunoGen and GenenTech. Right?
A. As there is with all of our contracts, yes.
Q. Another component of that agreement would have been IP,

intellectual property. Isn't that true?
A. That's also true.
Q. ImmunoGen had patents and pending patent applications at the time. Right?
A. Correct, on our maytansinoid technology.
Q. Right. And part of the deal is GenenTech could use technology in that space but needed to respect the patents, and if there was a product, pay royalties upon that product actually reaching the market. Right?
A. Correct.
Q. So that helped protect ImmunoGen so ImmunoGen would get the benefit of the bargain, that if a product came out of the collaboration, they would get some compensation for the hard work that they had put into the technology. Isn't that true?
A. That's true.
Q. And not all the patents that you had at the time had fully issued. At the time you entered the collaboration, some were still pending as applications. Isn't that true?
A. That is also true.
Q. And you realized that even if the patent issued much later, that it was still important intellectual property and you would have disclosed the application to GenenTech so that they knew about it and they knew that you potentially would be owed royalties on that patent even after it issued even if it was much later.

A. I can't fully -- I can't answer that question.
Q. You can't answer that question.
A. I'm not sure that GenenTech were privy to the -- the continuing patent applications or the activities of our intellectual properties until the patents issued. So I actually don't know the answer to that question.
Q. Now, one other aspect of a deal like this is another understanding. It flows from the confidentiality provision. And that's that the folks working on the project with you should not be using your information, using ImmunoGen's information, on another project. Right?
A. They shouldn't be using ImmunoGen's proprietary information.
Q. Right. The GenenTech scientists should not be using the ImmunoGen proprietary information that they got from the collaboration in some other project that was solely a GenenTech project. Right?
A. That's correct.
Q. That would be expected.
A. That would be expected.
Q. And you would expect them to have protocols in place to make sure that that happened. Right?
A. I'm not sure what the protocols were that were in place with those as a small company with a business development group of one. I don't know quite what you would mean by that.

But we all respected what was in the patents. I mean, the -- the license agreements.

Q. Yes. But my question to you is this. You would have expected, as one of the senior scientists at ImmunoGen, that GenenTech would have had protocols in place. Whether you knew they did or not, that would have been your expectation.

A. That would have been my expectation.

Q. Right. Now, Doctor, you've reviewed information on the collaboration between Seagen and Daiichi Sankyo. Right?

A. I have.

Q. And you realize that when they first embarked on this collaboration, Seagen was a much, much smaller company than Daiichi Sankyo. Right?

A. Correct.

Q. It was similar to ImmunoGen at the time, very small with new cutting-edge technology. Right?

A. Correct.

Q. And Daiichi Sankyo, even as its separate entities Daiichi and Sankyo, were big Japanese pharma companies. Right?

MR. RATLIFF: Objection Your Honor.

MR. CHIVVIS: Excuse me. I withdraw that.

Q. (BY MR. CHIVVIS) They were big --

MR. RATLIFF: Can we have a sidebar, Your Honor?

THE COURT: You objected to the question. He's withdrawn the question. Let's move on.

Q. (BY MR. CHIVVIS) Daiichi and Sankyo were big pharma companies. Right?

MR. RATLIFF: Objection, Your Honor. We still have the same issue, Your Honor, with respect to this particular question.

THE COURT: What's the basis of your objection that Daiichi Sankyo were big pharmaceutical companies?

MR. RATLIFF: Your Honor, we believe this goes to one of the rulings on the MILs.

THE COURT: Approach the bench.

(The following was had outside the hearing of the jury.)

THE COURT: If you're talking about agreed MIL No. 2 --

MR. RATLIFF: 2, yes, sir.

THE COURT: -- regarding total revenue profits, market cap size, calling it a big company doesn't violate that in my view. Going any more granular than that, might. But I'm going to overrule your objection.

MR. RATLIFF: Okay. And that's what I'm settling on, Your Honor. Thank you.

(The following was had in the presence and hearing of the jury.)

THE COURT: Objection's overruled. Let's continue.

Q. (BY MR. CHIVVIS) And I want to make sure that the

question was answered here.

Doctor Lambert, at the time Daiichi and Sankyo, and certainly after they merged together, were big pharma companies. Right.

A. I would have considered them big pharma companies from my vantage point at ImmunoGen at the time.

Q. Doctor, you reviewed documents related to the collaboration. Right?

A. I did.

Q. And you understand, of course, that Seagen disclosed the 2004 patent application to Daiichi Sankyo as part of that collaboration. Right?

A. I did.

Q. And you understand that Seagen would have had an expectation in that deal that its proprietary information wasn't used outside the scope of the collaboration. Right?

A. Correct.

Q. And you understand that Seagen would have had an expectation that Daiichi Sankyo would have had protocols in place to prevent the misuse of its confidential and proprietary information outside the scope of the collaboration. Right?

A. Correct.

Q. Now, in this case, did you talk to the individual Daiichi Sankyo scientists in working up the analysis that's reflected

in your reports?
A. No. I read -- I read materials.
Q. And did you talk to Doctor Agatsuma?
A. No, not in connection with any of this.
Q. You never asked him, did you, whether they had a protocol in place to prevent the misuse of Seagen's proprietary information outside the scope of the collaboration?
A. I didn't -- I didn't read anything about that. To my knowledge, they haven't.
Q. To your knowledge, they didn't actually have a protocol to prevent the misuse of Seagen's proprietary information. Right?
A. No, that's not what I said. I said to my knowledge they haven't used any of Seagen's proprietary information.
MR. CHIVVIS: Objection, non-responsive.
THE WITNESS: Okay.
THE COURT: Overruled.
Q. (BY MR. CHIVVIS) Doctor, my question is about whether there was a protocol.
A. I have no idea about Daiichi Sankyo's internal regulatory structures for how they conduct their business. I just read their scientific documents.
Q. So you have no idea whether they had a protocol to prevent the misuse --
A. I wasn't -- I wasn't --

THE COURT: Just a moment. Just a moment.

Doctor Lambert, you're going to have to let him finish --

THE WITNESS: Okay.

THE COURT: -- the question before you begin the answer. Otherwise, if you're both speaking at the same time, the record becomes confused and one of my important jobs is to make sure the record stays clear. So we all speak one at a time.

THE WITNESS: Thank you, Your Honor.

THE COURT: All right. Restate your question, counsel.

Q. (BY MR. CHIVVIS) Doctor Lambert, my question is focused here. You don't know and you did not investigate the question of whether Daiichi Sankyo actually had protocols in place to prevent the misuse of Seagen's proprietary information, did you?

A. That was not what I was asked to do.

Q. So you didn't do it?

A. So I didn't do it.

Q. Now, going back to ImmunoGen, in the early 2000s, and I think you even said this on one of your slides, ImmunoGen was known for a certain type of conjugation. Right?

A. Correct.

Q. Lysine conjugation. They used the lysine amino acids on an antibody as the spot they were connecting their drugs.

Right?
A. Correct.
Q. And ImmunoGen wasn't the only company doing lysine conjugation at the time. Isn't that true?
A. That's true.
Q. Many companies were using lysine conjugation at the time.
A. Certainly several, yes.
Q. In fact, Celltech and then Wyeth and later Pfizer were using lysine conjugation to connect antibodies -- excuse me, to connect drugs to antibodies.
A. That's correct.
Q. And other companies like Lilly from your slide were also using lysine conjugation.
A. Yes, they did, in the 1980s.
Q. In that early time frame of ADCs, lysine conjugation was more common for making ADCs than cysteine conjugation, wasn't it?
A. It was more common.
Q. And it's not solely associated with ImmunoGen, is it?
A. Lysine conjugation is not solely associated with ImmunoGen.
Q. Doctor, there are some problems with lysine conjugation, aren't there?
A. Lysine conjugation has strengths and weaknesses.
Q. One of the weaknesses is there are often over 70 lysine

amino acids on an antibody. Isn't that true?
A. It's thought to be a weakness, but it hasn't been in our experience.
Q. And, Doctor, I would really like a direct answer to my question. There are over 70 lysine amino acids on an antibody that, when you perform this conjugation, can be the attachment sites for the drug. Right?
A. That's true.
Q. And some of those lysines are actually at the -- let's call it the receptor site of the antibody that binds to the antigen on a target tumor cell. Isn't that true?
A. Sometimes.
Q. And if you do lysine conjugation, you might attach a drug right at that receptor site and then the antibody won't bind properly. Is that right?
A. It can happen.
Q. Doctor, in the early 2000s, there were concerns about whether cysteine conjugation could lead to successful ADCs. Isn't that right?
A. There was some concerns, yes.
Q. And one of the concerns was that cysteine conjugation could potentially destabilize the antibody because the cysteines were viewed as being necessary to the structure of the antibody. Right?
A. Yes, and it does destabilize -- reducing them does

destabilize some antibodies.
Q. So it sounds like you even have concerns about cysteine conjugation to this day.
A. Yes.
Q. But Seagen, I think you've said, is very well known for cysteine conjugation.
A. It is.
Q. And Daiichi Sankyo here is using cysteine conjugation. Right?
A. It is.
Q. I'd like to pull up slide 9 from Doctor Bertozzi's presentation earlier.
These are some of the early drug approvals in the ADC field, and I'd like to just walk through them and make sure we have a common understanding.
Now --
THE COURT: Counsel, there's no need to tell the jury what you'd like to do. Ask the witness questions.
MR. CHIVVIS: Yes, Your Honor.
Q. (BY MR. CHIVVIS) Doctor, mylotarg was one of the first ADCs to receive an approval. Correct?
A. True.
Q. And that ADC was technology originally developed at Celltech, and then there was some later relationship with Wyeth, and eventually Wyeth was purchased by Pfizer. Right?

A. That's my understanding.
Q. That ADC was withdrawn from the market after it was approved. True?
A. That's true.
Q. One of the problems was the acid cleavable linker that was used was unstable and there were toxicities. Right?
A. There were toxicities. I'm not sure they can all be ascribed to the linker.
Q. But you'd agree that that ADC was withdrawn and it was not reapproved until after Seagen and I believe GenenTech with Kadcyla received their approvals.
A. That's correct.
Q. The second ADC ever to be approved in the United States was Seagen's Adcetris. True?
A. That's also true.
Q. And the third was one of the ADCs that you had spent some time working on Kadcyla. Right?
A. That's also true, though there is another -- when mylotarg was approved in 2017, a drug called Besponsa was also approved, which is also a Pfizer drug.
Q. Yes. I'm just talking of --
A. On this list, yes.
Q. Moving forward on the dates here using this list, Doctor.
So you'd agree with me that Kadcyla was the third approved ADC. And at the time it was on the market, it was

only one of two on the market because it was Adcetris and Kadcyla. Mylotarg had been withdrawn.

A. Correct.

Q. And Seagen has received approvals on ADCs with its technology on three additional ADCs that have cysteine-conjugated, protease-cleavable linkers. Isn't that right?

A. That's correct.

Q. Those are Polivy, Padsev, and Tivdak. True?

A. True.

Q. And some of those ADCs treat blood cancers. Right?

A. Correct.

Q. And some of them treat solid tumors as well. True?

A. Two of them, yes.

Q. Doctor, you'd agree that Seagen has more approved ADCs on the market today than any other company.

A. Yes. It certainly leads the field.

Q. It certainly leads the field. That's what you said.

A. In number of approvals, yes.

Q. Now, ImmunoGen, again, has had one approval, and actually GenenTech holds the license for that approval. Isn't that right?

A. It does.

Q. And ImmunoGen, at least at a time, got a royalty for that. Right?

A. It did.
Q. Does ImmunoGen still get a royalty for it?
A. No. It sold the royalty stream to a royalty company in order to invest in its current product.
Q. So currently ImmunoGen is not even receiving royalty revenue on ADCs that it's gotten approved.
A. Not anymore.
Q. Since Kadcyla, ImmunoGen has not received another approval, has it?
A. That's correct, although a drug developed by ImmunoGen is now approved, but it's not an ADC.
Q. I'm focused on ADCs here, Doctor.
And the company hasn't done as well with respect to its stock in recent years, has it?
A. That's also true.
Q. Stock in the last four years has fallen by half or more.
A. Fallen depends on the starting point, but it's relatively low, yes.
Q. And when you retired in 2017, you retired holding substantial shares in ImmunoGen. Right?
A. I retired holding some shares, yes.
Q. And those shares are worth less today.
A. Compared to when I retired, it's about the same, actually.
Q. Well, this was mentioned in your opening remarks, but you

are getting compensated for this case. Right?
A. I am.
Q. You're getting paid $800 an hour in this case.
A. I am.
Q. And you're getting $800 an hour to testify against Seagen. Right?
A. No. I got $800 an hour to analyze the '039 Patent and be an expert witness.
Q. You are testifying against Seagen here today. Correct?
A. In the context of this proceeding, yes.
Q. And for every hour you're on the stand, you are getting paid for that time. Right?
A. Yes.
Q. And that's despite it being a company that your old friend Doctor Senter still leads as the head of chemistry. Right?
A. That's correct.
Q. I'd like to turn to your opinions on validity, Doctor. Can we do that?
A. Certainly.
Q. I'm going to -- I hope this is a simple question, but do you know what the legal standard is for invalidating a patent and who has the burden of proof?
A. I'm not a lawyer, so I can't really answer that question.
Q. You performed an analysis, Doctor, and you made a

determination that you think Seagen's '039 Patent is invalid. Right?

A. Yes.

Q. Don't you need to know what the standard is for invalidity and what -- who has the burden in order to make that determination?

A. The standard is in my report. And if I could look at the report, then I will be able to properly recite it to you.

Q. I've actually provided your reports, Doctor. I looked through them, and I did not see the standard for invalidity or who has the burden of proof. Do you recall seeing the standard in your reports?

A. No. That's why I asked to look. And if you tell me it's not there, it's not there.

Q. Doctor, if I asked you to state the standard you applied when you did your analysis, could you?

A. The standard I applied was to look at the entirety of the patent and then see if the claims were related to anything new in the patent.

Q. And, Doctor, if you were to think of the scales of justice. Right? And if you're -- with your analysis it's tipped slightly in favor of -- with your analysis that there wasn't, let's say, adequate disclosure in the patent, would it be your opinion that the patent's invalid?

A. Can you repeat the question, please?

Q. Let's think about the scales of justice. We have a little figurine right here. See the scales --
A. I do.
Q. -- on either side? Now, if -- is it your opinion that if the scales just tip slightly over to one side in favor of your view that there's not an adequate disclosure, that the patent's invalid?
A. I'm not sure what I can say to that. All I can say is that this -- what's -- what's new in the claim of this patent doesn't match what the description is in the specification. So --
Q. And you have no idea what the relevant standard is for doing that analysis.
A. Well, I would apply a common sense view that if it's not in the specification, there is nothing new in the specification, and the claim doesn't match what's new in the specification, then there should be no claim.
Q. Doctor, are you aware that patents are entitled to a presumption of validity?
A. I'm not a lawyer so I can't really answer that question yes or no.
Q. You don't even -- you have no awareness of that.
A. I'm told that patents have a presumption of validity, but I really don't know what their true legal standard is.
Q. Do you know why they have a presumption of validity?

A. You're asking me to speculate on a legal standard in an area that I'm not familiar with as -- as a non-lawyer.
Q. Doctor, I think you testified to this, but you examined the prosecution history in this case. Right?
A. I did.
Q. And you understand that the Patent Office has trained examiners that look at patents. Right?
A. I do.
Q. And they make sure that the patent meets the various legal requirements for a patent. Right?
A. I'm sure they do their best.
Q. They check to see whether it has an adequate written description. Right?
A. They should do that.
Q. And they check to see whether the claims are enabled. Right?
A. They should do that.
Q. And if prior art has been put before them that would sit in the time period between an earlier application and a later filing, they have to make an assessment of whether the priority claim is valid. Right?
A. I would expect that they should do that.
Q. And here you reviewed the patent history, the prosecution history, as we call it. Right?
A. I did.

Q. And so you know that the patent examiner here looked at the same Ogitani 2016 prior art reference that you've referred to and found that the patent should still properly issue. Right?
A. I'm not sure if my memory can accurately say whether the patent examiner considered the Ogitani reference. I know about the Ogitani reference myself because I read it separately because I read it separately as a paper. I can't remember if I also have looked at it in the file history.
Q. Doctor, one of the references you analyzed in your invalidity analysis, the analysis where you determined that the patent should be held invalid was Ogitani Clinical Cancer Research 2016. Right?
A. Yes, I'm familiar with the reference.
Q. And we can even show it on the screen here. That's PX 30. You recall this reference. Right?
A. I do.
Q. That's one of the references you say invalidates the patent. Right?
A. Yes, because of the date of its issue.
Q. And you know that the patent examiner actually considered this reference before she issued the '039 Patent. Right?
A. From my own recollection sitting here, I can't remember that.
Q. You didn't analyze it?

A. I can't remember that particular point.
Q. And you can't remember it being part of your analysis, either.
A. I can't remember that without referring to my analysis. If you could refer me to the document.
Q. Sure. I'll refer you to the prosecution history.
MR. CHIVVIS: If we could have PX 2 at 59.
THE WITNESS: And that's this folder here? Oh, you're going to show it to me.
Q. (BY MR. CHIVVIS) Yes. Doctor, do you know what an information disclosure statement is?
A. Yes.
Q. That's when a patent applicant having part of their duty of candor to be up front with the PTO --
A. Yes.
Q. -- submits documents to the PTO so they'll be considered by the PTO. Right?
A. Yes.
Q. Because they wants the PTO to actually look at the documents and issue the patent having considered them. Right?
A. Correct.
Q. And you see here Exhibit 59 is -- excuse me, Exhibit 2 at page 59 is an Information Disclosure Statement. Right?
A. I do see that, yes.
Q. And Seattle Genetics is the one that submitted this to

the Patent Office.
A. Yes, I do see that.
Q. And if we look down here, item No. 6, that's Ogitani Clinical Cancer Research 2016. Right?
A. Yes. That refreshes my memory.
Q. That's the same article we were just looking at.
A. Yes.
Q. It's the same article that you said invalidates the patent.
A. Yes.
Q. But the Patent Office actually was given it by Seagen in the course of prosecution. Right?
A. It was.
Q. And did you analyze this to determine whether the examiner considered this before making the argument that you're making to us all today?
A. I looked at -- I know you've refreshed my memory that I know it was in the patent history. So I assume that the patent examiner examined it closely, but I was not the patent examiner.
Q. Can you're not sure whether the patent examiner considered --
A. I would assume that the patent examiner did.
Q. Well, let's look just to be sure.
MR. CHIVVIS: If we could zoom in on the bottom of

the document here, Mr. Lee. It's actually a little bit farther down on the margin of the page than what you're showing, Mr. Lee. Right there at the bottom. And you've got to zoom in on the whole bottom. Yeah. There's some text at the very bottom so that block and the bottom. Yeah, there you go.

Q. (BY MR. CHIVVIS) So you see the examiner's signature there?

A. I do.

Q. Examiner's name is Christina Bradley. Right?

A. Yes.

Q. And she considered it in May of 2020. Right?

A. It would appear so, yes.

MR. CHIVVIS: And let's scroll down a little bit farther. There's another little line of text there. The previous page, bottom line of text on the -- it's right under there.

Q. (BY MR. CHIVVIS) Do you see where she wrote, All references considered except where lined through, CB?

A. I do see that, yes.

Q. Those are her initials there. Right?

A. Yes, I assume so.

Q. So let's look up on the screen. Did she strike through Ogitani to indicate she didn't consider it?

A. She did not.

Q. So this confirms, in fact, that the examiner considered the very argument you're making to say the patent's invalid. Right?
A. Yes, this document supports that statement.
Q. And then she issued the patent after that. Right?
A. Evidently, yes.
Q. Doctor, let's look at the specification of the '039 Patent that we've been talking about today.
Now, it's your opinion that there is no support in the patent for a tetrapeptide with G and F. Right?
A. There's no support for a G/F-only tetrapeptide.
Q. But -- now, the claim doesn't use the word 'only', does it?
A. It doesn't have to. The full G/F-only is just shorthand for what the whole claim is.
Q. Doctor, I'm going to be very specific with this question. Yes or no, does the patent use the word 'only' in the claim to refer to the G and F limitation?
A. No, it doesn't.
Q. Okay. And it does require a tetrapeptide, though. Right?
MR. CHIVVIS: Let's look at Plaintiff's 1. This is going to be at 80 of the PDF, Mr. Lee, column 65.
Q. (BY MR. CHIVVIS) This is the formula that the patent gives for the peptide unit. Right?

A. It's a description of all the peptides -- all the peptides that are possible from dipeptides to 12-unit peptides, and it gives a description of the structure of the amino acids that could comprise the peptide building blocks.
Q. You were here when Doctor Senter testified about the discovery of this invention. Right?
A. I was.
Q. And despite not being as close as maybe you once were, you still take Doctor Senter's word, don't you?
A. I do.
Q. And you understand that Doctor Senter said that what his team discovered was a broad invention. Right?
A. I heard him say that, yes.
Q. So when they made that initial discovery in 2004, they weren't at the time limiting themselves to G- and F-only tetrapeptides. Right?
A. They didn't discover any peptides here, any tetrapeptides.
Q. Doctor, you heard Doctor Senter's testimony. Right?
A. I heard Doctor Senter's testimony, yes.
Q. And he testified that they found almost any peptide would cleave in a protease cleavable linker when they tested them. Right?
A. I did hear him say that.
Q. Okay. And here there is a disclosure of tetrapeptide.

MR. CHIVVIS: Let's highlight that, Mr. Lee.
Q. (BY MR. CHIVVIS) That's the word in the claim, and it is disclosed right here. Right?
A. You've added the blazemark, but it is disclosed there, yes.
Q. Okay. You agree with me, Doctor Lambert, that the word 'tetrapeptide' appears in the disclosure of the patent.
A. Yes.
Q. And then there is a formula. Do you see that?
A. Yes.
Q. And the chemical diagram on the left with that R19, that's actually a formula for an amino acid backbone. Right?
A. It is.
Q. And if you substitute out that R19 with different chemical molecules as listed below, you get different amino acids. Right?
A. Yes.
Q. And so what the inventors were reciting here is that you could have a tetrapeptide, they showed the amino acid backbone, and then they disclosed the various different amino acids that could fit -- fill that R19 and -- and create that chain of amino acids. Right?
A. Yes, they disclosed a lot of amino acid side chains.
Q. And one of the side chains that they disclosed was hydrogen. Right?

MR. CHIVVIS: Can we highlight that, Mr. Lee?

THE WITNESS: Yes. I can see that.

Q. (BY MR. CHIVVIS) And hydrogen, if we were to put that where the R19 goes, that would create an amino acid glycine, which we call G.

A. Correct.

Q. There's another molecule here, benzyl.

MR. CHIVVIS: Can we highlight that, Mr. Lee?

Q. (BY MR. CHIVVIS) And if we were to take that one and put it in the R19 there, we get the amino acid phenylalanine, or F. Right?

A. That's correct.

Q. So what the inventors disclosed here is a formula where from the options you could select is a tetrapeptide. Do you see that?

A. Yes.

Q. And then they gave the formula for the specific amino acid backbones of a peptide sequence. Right?

A. Yes.

Q. And then they told the world that the amino acid could be glycine or could be benzyl. Right?

A. Yes, amongst others.

Q. Now, you would agree with me then that the inventors disclosed tetrapeptides that could include glycine and phenylalanine. Right?

A. Amongst others, yes, in principle.
Q. And, in fact, they disclosed a specific tetrapeptide in which three of the four amino acids were glycine or phenylalanine. Right?
A. They did.
Q. And so if we look at the claim language and specific words used in the claim, we see tetrapeptide. Right?
A. Yes.
Q. We see that amino acid backbone. Right?
A. Yes.
Q. We see hydrogen. Right?
A. Yes.
Q. We see benzyl. Right?
A. Yes.
Q. And that all appears in the '039 Patent. Right?
A. Yes.
Q. In the disclosure of the '039 Patent.
A. Yes, without the highlighting.
Q. And those exact same words appear in the original application that Doctor Senter and his co-inventors filed in 2004. Isn't that true?
A. That's true.
Q. Now, Doctor Lambert, synthesizing peptides has become fairly routine since the early 2000s. Right?
A. Yes.

Q. Even in the early 2000s, it was routine.
A. Yes, I would say that.
Q. There are synthesis machines that you program in the peptide sequence you want and it will just make it for you. Right?
A. That's correct.
Q. And if you have a number of those machines, you can make a lot of peptides in parallel. Right?
A. Yes.
Q. You can make hundreds.
A. Yes.
Q. And it wouldn't take that long.
A. It wouldn't take that long.
Q. And here we have a claim directed to 81 tetrapeptides --
A. That's correct.
Q. -- of G and F combinations.
A. Correct.
Q. You'd agree with me that those could be made in the lab very quickly.
A. They could if you knew that you had to make them.
Q. If you wanted to make a hundred G and F tetrapeptides, you could do it in a week.
A. I expect you could.
Q. And you could have done it in a week in 2003?
A. I expect you could.

Q. And even as of 2003, if one had reason to make a G and F tetrapeptide for some application, a POSA would have been able to make and analyze those tetrapeptides, wouldn't they have?
A. If you had a reason, the POSA would have been able to make them and analyze them.
Q. And when we say the term POSA, what are we referring to?
A. A person of ordinary skill in the art. It's an acronym.
Q. And that's the lens you're supposed to view the patent through. Right?
A. Yes, it is.
Q. So it wouldn't have been -- withdrawn.
Doctor, we talked about how the BMS technology was all licensed to Seattle Genetics. Seattle Genetics was basically a spin-out founded on that nucleus of technology that was first developed at BMS?
A. Yes.
Q. And are you familiar with the work of Doctor Dubowchik?
A. Yes, I am.
Q. And have you read his paper on an amino conjugate of camptothecin?
A. Yes, I have.
MR. CHIVVIS: Let's pull up PX 155.
Q. (BY MR. CHIVVIS) Are you familiar with this paper?
A. I am.
Q. And this paper was based on work done in the late '90s by

Doctor Dubowchik and team. Right?
A. Yes.
Q. And what Doctor Dubowchik demonstrated, you could attach a camptothecin to a peptide cleavable linker and attach that to an antibody. Right?
A. Yes.
Q. And, again, just to be clear, Seagen is the spiritual successor of the BMS work. Right?
A. Yes. The Val Cit dipeptide came from BMS work.
Q. But the spin-out wasn't limited to Val Cit, was it?
A. It was not.
Q. Doctor, by 2003, the chemistry for attaching many different drug moieties to an ADC was known. Right?
A. I would disagree with that. No.
Q. Doctor, the chemistry for attaching minor groove binders, DNA binders like calicheamicin, were both known by 2003. Right?
A. What was known was to attach specific drugs that had specific functional groups, attachment groups, if you like. But there would be other drugs that would have those general classes that were probably unlinkable.
MR. CHIVVIS: Objection, non-responsive.
THE COURT: Overruled.
Q. (BY MR. CHIVVIS) Doctor, you'd agree with me that calicheamicin was a drug that had been successfully attached

to an ADC by 2003. Right?
A. Yes.
Q. You'd agree with me that a minor group binder had been successfully attached to a drug -- excuse me, successfully attached to an antibody as of 2003. Right?
A. Yes.
Q. You'd agree with me that camptothecin had been successfully attached to an antibody in an ADC by 2003. Right?
A. Right.
Q. You'd agree with me that a maytansinoid, such as DM1, had been successfully attached to an antibody by 2003. Right?
A. Right.
Q. You'd agree with me that doxorubicin had been successfully attached to an antibody as of 2003. Right?
A. Right.
Q. All of those drugs had been successfully attached to antibodies as of 2003. Right?
A. Correct.
Q. Doctor, I'd like to pull up your slide No. 37.
Now, in this slide you attribute cysteine conjugation to CytoGen and NeoRx. Right?
A. Right.
Q. And to be clear, CytoGen has never made an FDA-approved ADC. Right?

A. Right.
Q. Neither has NeoRx.
A. Correct.
Q. Let's pull up your slide No. 39. Remember this slide?
A. I do.
Q. This is part of your explanation for why in Daiichi Sankyo's laboratory notebooks, when they're making the molecules that led to the development of DS-8201, Enhertu, it was okay for them to say SG-type. Right?
A. When I looked at all of that, it seemed to be the context of a shorthand way of describing cysteine conjugation, yes.
Q. But not any cysteine conjugation. Right? You say here on your slide Seagen's Adcetris SG-type cysteine conjugation. Right?
A. Actually it is any cysteine conjugation because there are only certain cysteines in any antibody.
Q. Well, wait a minute.
A. Adcetris was just the first compound that was an FDA-approved drug using that cysteine conjugation method.
Q. The first compound to validate the cysteine conjugation method. Right?
A. There are many things that go into validation to end up with an approved drug.
Q. And Adcetris validated cysteine conjugation. Right?
A. I would disagree.

Q. Okay. So SG, does that stand for something general-type cysteine conjugation?
A. No. It -- I mean, I take it as standing for Seattle Genetics-type conjugation.
Q. Well, wait a minute. Let's go back to your slide No. 37. I thought you said CytoGen came up with cysteine conjugation.
A. They did.
Q. Well, why don't we call it CytoGen-type conjugation then?
A. I assume because CYTOGEN didn't develop a potent drug to be able to make an ADC that was effective.
Q. So your opinion is that CytoGen claims the fame to cysteine conjugation, but we don't call it CytoGen-type conjugation, do we?
A. They didn't gain any fame because they didn't develop a successful drug.
Q. And we don't call it NeoRX conjugation or NR conjugation, either, do we?
A. We do not because they never developed a successful drug, either.
Q. It's Seagen-type conjugation that Doctor Miyasaki was referring to in his laboratory notebook, isn't it?
A. It is.
Q. Doctor, I'd like to pull up your slide No. 8. Do you remember this slide?
A. I do.

Q. This traceless cleavable linker and non-traceless cleavable linker?
A. Correct.
Q. And then you have a diagram on the left that actually looks a lot like Doctor Bertozzi's diagram. Right?
A. Yes. It's showing cleavage between the peptide and the spacer drug.
Q. But you add these concepts of traceless cleavable linker and non-traceless cleavable linker?
A. Uh-huh.
Q. Now, you didn't show us --
THE COURT: Just a minute. You'll have to answer yes or no. Non-verbal answers don't translate in the record. Go ahead, counsel.
THE WITNESS: Sorry. That -- that was a yes.
Q. (BY MR. CHIVVIS) You didn't show us Seagen documents that used the terms traceless or non-traceless cleavable linker. Right?
A. I didn't.
Q. And you didn't show us Daiichi Sankyo documents that used the terms traceless cleavable linker and non-traceless cleavable linker.
A. I didn't.
Q. And you didn't show us in the patent where in the claims there's any requirement for a traceless cleavable linker or a

non-traceless cleavable linker, either, did you? Those words don't appear in the patent.

A. Those words don't appear in the patent.

Q. They don't appear in the claims and they don't appear anywhere in the specification. Right?

A. The word 'traceless' does not appear anywhere in the specification.

Q. And the word 'non-traceless' doesn't appear, either, does it?

A. It does not.

Q. But it's your position that this is the critical feature that we all need to analyze to understand whether there's infringement in this case. Right?

A. Yes.

Q. And coming from this feature, you make two conclusions. Right?

A. Yes.

Q. One, that no free drug gets released from Enhertu. Right?

A. That's correct.

Q. So you use this traceless/non-traceless construct to make that argument about free drug. Right?

A. The traceless/non-traceless is a construct to describe unmodified or modified drug moities when they're released.

Q. But the actual claim -- interpreted claim language that

we're talking about here just says free drug. Right?
A. It does say free drug.
Q. Right. So that's the requirement that we're looking at whether is met or not, and you're using this construct to say it's not met.
A. I am.
Q. Okay. And you're also using the exact same construct to say that the linker in Enhertu is not self-immolative.
A. Yes.
Q. Well, let's look at that for a moment. And I'd like to put up your slide 28 just so it's really clear what your position is here.
You see you've got the same construct shown on the bottom. Right?
A. Yes.
Q. This traceless/non-traceless idea. But now you've zeroed in on some claim language, self-immolative.
A. Yes.
Q. And just to be clear, self-immolative only appears in a dependent claim of the patent. Right?
A. Yes.
Q. So even if you were right about this, that wouldn't affect whether Enhertu infringes claim 1 of the patent. Right?
A. My understanding is that the Court interpreted drug

moiety being fully released as being the release of the free drug.

Q. We can go into the claim constructions in a second. But on your opinion on self-immolative, that whether that element is met or not, only goes to claim 3. The words 'self-immolative' do not appear in claim 1. Right?

A. The word 'self-immolative' does not occur in claim 1. Correct.

Q. Okay. You reviewed the FDA submissions of Daiichi Sankyo in this case. Right?

A. I looked at some of the documents that were submitted to FDA by Daiichi Sankyo, yes.

Q. And you've been here throughout this whole trial. Right?

A. I have.

Q. And you heard the testimony of Daiichi Sankyo's global team lead -- excuse me, global regulatory team lead, Amita Chaudhari. Right?

A. I did.

Q. She's in charge of the FDA documents. Right?

A. I understand that she was.

Q. And as part of that process, in her testimony you heard in court and the testimony you reviewed when you were doing your analysis, you saw that she described that Daiichi Sankyo has a robust process for ensuring the accuracy of the documents it submits to the FDA. Right?

A. I did hear that, yes.
Q. Because this is the FDA we're talking about. Right? You've got to make sure the information is accurate.
A. Yes.
Q. It's really important when you're seeking approval for a medicine that you tell the truth to that agency. Right?
A. That's correct.
Q. So let's look at whether Daiichi Sankyo, with the molecule that is Enhertu, has a self-immolative spacer.
MR. CHIVVIS: Could we get PX 163? And let's go to page -- okay. Actually we'll wait here.
Q. (BY MR. CHIVVIS) You understand that this is part of the FDA submission for the approval of Enhertu?
A. Yes, I do understand that, yes.
MR. CHIVVIS: And let's go to page 6.
Q. (BY MR. CHIVVIS) Okay. And you see here there's a discussion of antibody-drug conjugate design?
A. Yes, I see that.
Q. And it's talking about the design of --
MR. RATLIFF: One moment. Your Honor, we're starting to get into confidential information here displaying --
THE COURT: Are you requesting that I seal the courtroom?
MR. RATLIFF: Yes, please.

THE COURT: All right. Based on counsel's request and to protect proprietary information, I'll order the courtroom sealed.

Those present not subject to the protective order in this case should excuse themselves and remain outside the courtroom until the Court reopens and unseals the courtroom.

(Courtroom sealed.)

(Courtroom unsealed.)

THE COURT: The jury is excused for recess.

(Whereupon, the jury left the courtroom.)

THE COURT: The Court stands in recess.

(Brief recess.)

THE COURT: Be seated, please.

MR. CHIVVIS: Your Honor, before we call back in the jury, Plaintiffs would like to offer the exhibit made in cross-examination of Doctor Lambert as Plaintiff's 2000.

MR. RATLIFF: Objection, Your Honor. Plaintiff's have already passed the witness, and I'd like to continue my examination.

THE COURT: We're not going to pre-admit exhibits in the middle of the trial.

MR. CHIVVIS: Okay.

THE COURT: I'll overrule that request. It's a demonstrative. It's proper for use in closing, but it's not an admitted exhibit.

MR. CHIVVIS: Thank you, Your Honor.

THE COURT: The testimony by the witness about it is certainly evidence in the case.

Are you prepared to go forward with redirect, Mr. Ratliff?

MR. RATLIFF: I am, Your Honor.

THE COURT: All right. Doctor Lambert, if you'd return to the witness stand, sir, and, as you understand, you remain under oath.

THE WITNESS: Thank you, Your Honor.

THE COURT: You're quite welcome.

All right. Please bring in the jury, Mr. Latham.

(Whereupon, the jury entered the courtroom.)

THE COURT: Please be seated, ladies and gentlemen. We'll continue with the examination of Dr. John Lambert, and the Defendant will now proceed with redirect.

Mr. Ratliff, you may proceed.

MR. RATLIFF: Thank you, Your Honor.

REDIRECT EXAMINATION

BY MR. RATLIFF:

Q. Doctor Lambert, you recall being asked questions about this document. Right?

A. I do.

Q. And let me just make sure it's straight.

And I want to first talk about the elements. You recall being asked questions about the elements in Seagen's patent claim?

A. I do.

Q. And let's turn to the first element. And looking at the first element, sir, which is the antibody. Do you see that?

A. I do.

Q. And has an antibody ever been considered Seagen's proprietary technology?

A. No, it hasn't.

Q. And, sir, can you tell us, when have antibodies been used in ADCs?

A. For a long time. Since the early 1980s.
Q. Now, so this has never been Seagen's proprietary technology. Correct?
A. No.
MR. CHIVVIS: Objection; leading.
THE COURT: Avoid leading, counsel. This is redirect.
MR. RATLIFF: Understood, Your Honor.
THE COURT: Sustain the objection.
Q. (BY MR. RATLIFF) And so this is never -- in your opinion, can you tell us, has this been Seagen's proprietary technology, an antibody?
A. No. Antibodies are not proprietary to any ADC company.
Q. Okay. Now, let's go to the second element, conjugation to sulfur atom on cysteine in an antibody. You recall being asked questions about that.
A. I do.
Q. Now, has conjugation to a sulfur atom on a cysteine in an antibody ever been proprietary to Seagen?
A. No, it is not.
Q. To your knowledge, does Seagen have any patents on that technology?
A. No, it doesn't.
Q. And can you explain to us, when was that technology available in the public domain for people to use?

A. In the early 1980s.
Q. And, Doctor Lambert, when you first started doing work on this case, were you surprised that Seagen was trying to portray the use of conjugation to a sulfur atom on a cysteine in an antibody as Seagen's proprietary technology?
A. As a protein chemist, I have been conjugating or reacting cysteines in proteins since my Ph.D. It is just standard protein chemistry.
Q. Now, I'd like to go to the next element that we see in the claim, which is the MC unit.
Now, you recall being asked questions about this, Doctor?
A. I do.
Q. And has using an MC unit ever been Seagen's proprietary technology?
A. No, it has not.
Q. And can you explain to us when, before Seagen was even formed, people in the industry were making ADCs with MC groups?
A. In the early '90s and probably the late 1980s.
Q. And when you started your work on this case, were you surprised that Seagen was trying to portray as its own proprietary technology use of an MC unit?
A. I was very surprised, yes.
Q. Now, Doctor Lambert, let's go to the next element, which is the tetrapeptide of G and F. Now, this is a -- is this a

tetrapeptide of G and F only?
A. Yes, that's my understanding.
Q. And you recall being asked questions about this. Correct?
A. I do.
Q. And you've heard the testimony from Doctor Senter, Doctor Bertozzi, and others, have you heard anyone within Seagen ever claim that they first came up with a G and F only tetrapeptide in an ADC?
A. I have never heard anyone say that.
Q. And you, in fact, before hearing the testimony of -- let me start over. Let me withdraw that.
In this case, did you hear testimony from Doctor Senter explaining that the first time he saw a G and F only tetrapeptide in the ADC was Enhertu?
A. Yes, I do recall that, and it was the first time I saw it as well.
Q. And did you hear any testimony from anyone else from Seagen about the first time that they saw a G and F only tetrapeptide was in Daiichi Sankyo's Enhertu?
A. I did hear that several Seagen scientists so testified.
Q. And so this element of the claim, in your opinion, has it ever been proprietary to Seagen?
A. No, it has not.
Q. Has it ever been an element that Seagen even thought of?

A. No, it didn't.
Q. And was it an element that was in the 2004 application?
A. No, it wasn't.
Q. Now, let's go to the spacer element. Now, do you recall being asked questions about the spacer unit?
A. I do.
Q. And has using a spacer unit ever been the proprietary technology of Seagen?
A. No, it hasn't, though they did license a particular spacer from Bristol Myers Squibb.
Q. And what was that particular spacer?
A. That particular spacer is known as PABC, short p-aminobenzyl carbamate. It is used in Seagen's inhibitor products that use a cleavable linker.
Q. And can you tell the jury if that spacer is similar to the spacer that's actually in Enhertu?
A. A completely different chemical.
Q. And what do you mean by in a? Is it completely different chemical and does it function differently?
A. It's a completely different chemical structure, and it's function is different in that, in the Seagen compound, the PABC spacer completely falls off and releases free drug--in that case, MMAE, or the auristatin drug, in their products. And in Enhertu, the spacer is -- only partially falls off and is part of the spacer remaining. So even functions in a

different way.
Q. So, Doctor, has use of a spacer unit in an ADC ever been proprietary or owned by Seagen?
A. They didn't invent the use of spacers in ADCs.
Q. So, Doctor, let's go to the next element which is the p ranges. This relates to the DAR. Is that right?
A. That's correct.
Q. And you recall being asked about this. Right, sir?
A. I do.
Q. And has using a DAR ever been proprietary to Seagen?
A. Not that I'm aware.
Q. And were people measuring DAR and did ADCs have DARs before Seagen was even formed?
A. Certainly, yes.
Q. And are you -- were you surprised when you first started working on this case that Seagen was trying to claim the use of a DAR as its own technology?
A. Yes.
Q. Now, Doctor, you recall being asked lots of questions about D being a drug.
A. Yes.
Q. And when you were asked those questions, do you recall that you were being asked questions in reference to documents that Daiichi Sankyo had submitted to the FDA?
A. I do.

Q. And in your answers, do you recall saying that there was context?
A. I do.
Q. And can you explain to us what it means when you say that there's context for the references in those BLA documents?
A. So the context is that in the BLA documents, which is describing the behavior of Enhertu in animal -- in animal testing, especially from the point of view of safety pharmacology, what the pharmacologists are interested in and what they're communicating to the FDA safety pharmacologists is what is the free drug relative to bound drug that is intact Enhertu.

So the word free in that context just means whatever actually has come off Enhertu in an animal, ultimately in a patient.

Q. And can you explain to the jury if this -- the statements that you were shown in the BLA have anything to do with the context of the drug moiety that's referenced in Seagen's patent?
A. No. I think the reference, the drug moiety, in the claim is a very precise definition that is and has been construed to mean free drug without any elements of the linker attached.
Q. Now, let's talk about this last element--intracellularly cleaved to release free drug. Do you see that?
A. I do.

Q. And you recall being asked questions about it?
A. I do.
Q. And here is the context in which the BLA documents discuss the release of the drug moiety in Enhertu different than the context that the '039 Patent talks about it?
A. Yes, it is.
Q. And can you explain to us the differences?
A. So in the BLA, the context is that it's free drug, not bound. But in the context of the claim, it means that the drug moiety must be intracellularly cleaved and releasing free drug without any elements of the linker attached.
Q. Now, Doctor, all of these elements that are here in the claim, do they have to be, in your opinion, taken together and considered as a whole?
A. Yes. The claim isn't to an MC group or to a peptide. The link -- the claim is to an entire ADC as a whole; then, furthermore, where the drug moiety has to intracellularly cleave in a patient. And so that is the claim. It has to be viewed as the whole ADC.
Q. Now, Doctor Lambert, you recall being asked questions about this claim as a whole. Correct?
A. I do.
Q. And do you also recall hearing from Doctor Senter, a named inventor on this patent, having never seen an ADC that falls within this claim until he saw Daiichi Sankyo's drug,

Enhertu? Correct?

A. I did hear him so testify.

MR. CHIVVIS: Objection, leading.

THE COURT: Sustained. Avoid leading on redirect, counsel.

MR. RATLIFF: Understood, Your Honor.

Q. (BY MR. RATLIFF) So, Doctor Lambert, do you recall that when you heard from some testimony from Doctor Senter, that Doctor Senter explained that he had never seen an ADC falling within the claims?

MR. CHIVVIS: Objection, leading.

THE COURT: Sustained. A question that calls for a simple yes or no where you supply the answer in the question is classic leading, and it's not permitted on direct examination.

MR. RATLIFF: Understood, Your Honor.

Q. (BY MR. RATLIFF) Now, Doctor, with respect to this entire claim, do you recall any testimony from anyone that was a named inventor about whether or not they saw an ADC that fell within this claim?

A. Yes. I recall that Doctor Senter, who is a named inventor on this patent, testified that he'd never seen a G/F-only tetrapeptide in any ADC until he saw the presentation by Daiichi in December 2015.

Q. And, Doctor Lambert, can you tell us whether in the

entire existence of Seagen as a company, have they ever created an FDA-approved ADC that falls within this claim?

A. No, they haven't. All of Seagen's approved ADCs would actually be outside this claim.

Q. And, Doctor Lambert, based upon the information that you've seen in this case, did Seagen write this claim before or after seeing Daiichi Sankyo's product Enhertu?

A. They filed this claim after seeing the product Enhertu.

Q. Now, Doctor Lambert, I'd like to bring up --

THE COURT: Just a minute, counsel.

Let's take a short recess. I'm going to excuse the jury.

(Whereupon, the jury left the courtroom.)

THE COURT: Counsel, approach the bench.

Be seated, please.

(The following was had at the bench.)

THE COURT: Counsel, I'm told by the court staff that Juror No. 4 threw up just before they returned to the last recess and she looked like she was about to throw up again. That's why I sent the jury out. I have no idea if it's something she ate or something different.

I've asked the deputy in charge to check with her during this recess, and we'll see where we are. But I wanted to explain to you why we just did what we did. Okay?

MR. RATLIFF: Thank you, Your Honor.

(The following was had in open court.)

MR. CHIVVIS: Your Honor, while the jury's out, may I be heard on two points?

THE COURT: I don't see why not, Mr. Chivvis.

MR. CHIVVIS: Thank you.

THE COURT: If you'll go somewhere where you can amplify your voice, please.

MR. CHIVVIS: Yes, sir.

Your Honor, we have two overarching concerns with the line of questioning on redirect.

One, and I was cautious not to interrupt counsel while he was asking the questions, was that counsel seemed to even step over the line that was earlier drawn on what the constructions were and had the witness push the envelope on that, actually reciting the witness' view that the claims were construed to be a certain thing. And I thought that that testimony could be very confusing to the jury.

Second, and most recent, is that counsel started to imply that there's something improper about filing a patent claim that reads on a competitor's product. We dealt with this issue in in limine practice, Your Honor, and that's supposed to be off limits. So we're concerned about that.

I didn't want to interrupt the testimony, but given the break, I thought that this was an appropriate time to raise both issues.

THE COURT: Do you have a short response, Mr.

Ratliff?

MR. RATLIFF: Yes, I do, Your Honor.

On the question regarding the claim scope, counsel was free to do a redirect and counsel questioned the witness extensively about his opinions and interpretations of the claim.

THE COURT: You mean on cross-examination.

MR. RATLIFF: On cross-examination.

And, secondly, Your Honor, the simple question that I asked about the timing did not give any implication. It's just the facts.

THE COURT: Well, you need -- let me say this. Use of the word 'construed' with the witness, when you're addressing claim language, calls for real precision, and if it varies from the actual construction of the Court at all, then it's improper.

Now, where the Court has not construed a term, the witness can certainly testify about its plain and ordinary meaning. But it seems to me, and we've discussed this at the bench already, that there is a dispute about the degree of degrading that needs to take place to free the drug from the linker. And the construction of self-immolative spacer that the Court's adopted provides that the spacer will spontaneously degrade to release the drug.

You've taken the position it must completely degrade so

that there's no portion of the spacer still connected to the drug. Plaintiff's taken the position that as long as the drug is freed from the linker and there is adequate degrading to release the drug, then it meets the construction of the That's an issue that the Court did not address in its construction--the extent of the degrading. The Court simply construed the term to require degrading.

It is ultimately, in my view, for the jury to decide whether degrading that is less than complete, as Defendant argues, is adequate to comply with the Court's construction, or whether degrading that frees the drug but still leaves some portion of the linker attached but frees the drug from being immobilized by the linker is adequate to meet the Court's claim construction.

Given that the Court's claim construction says degrades to release, I view that as an issue the jury's ultimately going to have to decide. And both you gentlemen can argue it and examine and cross-examine this witness and other appropriate witnesses to the fullest extent you believe is appropriate.

But I don't want anybody to characterize their particular view on that issue as the Court's construction, because the Court's construction does not specifically address the extent of the degrading necessary. It simply says degrades to release. And, therein, in my view, is the rub, and we have an

issue that ultimately the jury's going to decide.

So argue it, cross-examine and examine the witness as adequately on the point, but don't represent to the jury that the Court has adopted either of your views of either party on that issue. Understood?

MR. RATLIFF: Understood, Your Honor.

THE COURT: Does that address your question, Mr. Chivvis?

MR. CHIVVIS: Thank you, Your Honor. It does.

THE COURT: All right. Why don't you have a seat. We'll see where the jury is in just a minute.

(Pause in proceedings.)

THE COURT: Counsel, I'm going to recess for just a minute. We'll come back as soon as I understand what's happening with Juror No. 4.

(Brief recess.)

THE COURT: Be seated, please.

Counsel, let me confirm on the record what I just told you in chambers. It's obvious to those of us in the courtroom that one of our jurors was nauseated and immediately had to leave the courtroom at the time I called the last recess. It's difficult to know at this point what cause, minor, serious, or somewhere in between, that might be.

We are at 10 minutes or so after 5:00. I'm going to send the jury home for the rest of the day. We'll bring them back

in the morning. If that juror gets worse overnight and can't appear tomorrow, it's my intention to excuse her and to go forward with six jurors. If overnight she improves and can come back and serve tomorrow, then we will continue tomorrow morning with all seven jurors.

Any questions from either Plaintiff or Defendant about that?

MR. HILL: No, Your Honor.

MR. MANN: None from the Defendants, Your Honor.

THE COURT: All right. Here's Ms. Clendening, our Deputy-in-Charge. Ms. Clendening, will you go to the jury room, tell the jury that they're excused for the evening, tell them I expect to see them back ready to go by 8:30 in the morning, and remind them to follow all my instructions about their conduct? Will you do that for me? Please do that right now.

All right. With that having been accomplished, counsel, we will pick up in the morning where we left off with Doctor Lambert this afternoon. And until that time, we stand in recess.

(The proceedings were concluded at 5:10 p.m.)

I HEREBY CERTIFY THAT THE FOREGOING IS A CORRECT TRANSCRIPT FROM THE RECORD OF PROCEEDINGS IN THE ABOVE-ENTITLED MATTER. I FURTHER CERTIFY THAT THE TRANSCRIPT FEES FORMAT COMPLY WITH THOSE PRESCRIBED BY THE COURT AND THE JUDICIAL CONFERENCE OF THE UNITED STATES.

S/Shawn McRoberts 04/06/2022

_____DATE_____

SHAWN McROBERTS, RMR, CRR
FEDERAL OFFICIAL COURT REPORTER